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COVID's Missing Element: Pathogenesis and Treatment Revealed

welcome to the lenny and Maria sanchez deep dive podcast show.

Lenny: Today, we're delving into a fascinating perspective on COVID-19, exploring insights from a KZN doctor's experience treating patients in an outpatient setting. Our first point comes from Source 1, which highlights the current limitations in understanding COVID-19 disease progression and the scarcity of outpatient treatment recommendations. It also points out the controversy and confusion surrounding the pathogenesis and treatment of the virus, despite a wealth of information from hospital settings.

Maria: Moving on to Source 2, we learn about the doctor's direct experience. Over five months, his staff and he examined, treated, and followed up on more than 200 symptomatic COVID patients, including some critically ill individuals. This hands-on approach allowed him to refine his understanding of COVID pathogenesis and adjust treatment protocols, leading to remarkable and consistent recoveries, with no deaths or hospitalizations among his patients.

Lenny: Our next key insight is drawn from Source 3. This source emphasizes that the information gathered from treating patients can significantly prevent COVID-related mortality and morbidity. It also provides fundamental details about the virus, describing it as an RNA virus, transmitted airborne, with potential for waterborne spread through stool samples. The source notes the virus's high contagiousness, but underscores that its infectivity and virulence remain unclear due to testing limitations and a lack of understanding of its pathogenesis. It clarifies that the virus enters cells via ACE2 receptors, replicates, and causes cell debris and inflammation, with symptoms typically lasting 3 to 6 days.

Maria:Source 4 brings up important considerations regarding laboratory detection. It points out that the ability of swabs to isolate the virus varies greatly due to factors like technique and training. PCR tests, while very specific, are not very sensitive, with about a 35% false negative rate, making them unreliable for diagnosis or confirmation. Therefore, PCR tests are deemed useful only for screening, not sensitive enough to guide isolation or quarantine. The source suggests that absolute numerical data may not reflect the true picture, and antibody testing might provide more reliable data.

Lenny: From Source 5, we gain insight into the observed clinical presentation of COVID-19. Symptoms often begin with upper respiratory tract infection, including a sore throat, loss of smell, and taste changes, alongside generalized body ache, fever, and chills. The infection can then spread lower, causing a dry persistent cough, a cold feeling between shoulder

blades, chest burning, and tightness with clear sputum. The source also notes the possibility of bacterial co-infection, leading to a productive cough with purulent sputum, sinusitis, and earache. These symptoms are described as progressing over the first six days of infection.

Maria: Our sixth key takeaway, found in Source 6, presents the doctor's central hypothesis. Based on his broad natural science background and experience, he believes that COVID illness has two distinct etiologies: an initial respiratory viral infection with typical symptoms, and a later triggering of a Type 1 hypersensitivity reaction in sensitive individuals. This article, he explains, delves into both the pathogenesis of COVID and his outpatient treatment protocols.

Lenny:Source 13 elaborates on a critical phase of the illness: the development of dyspnoea. A significant proportion of infected individuals experience dyspnoea from day 7 onwards, regardless of their initial symptom severity. This dyspnoea can be sudden and rapidly progressive, leading to severe hypoxaemia and a sharp drop in SpO2, or it can be insidious and persistent, potentially resulting in diffuse lung fibrosis. It is during this period, the source notes, that rashes, neurological symptoms, and end-organ damage are also commonly reported.

Maria: Moving to Source 19, it becomes clear why a single viral infection is insufficient to explain the observed COVID-19 symptoms. This source argues that the diversity of symptoms, unusual presentations, and outcomes seen in COVID-19 cannot be attributed to a viral infection alone. Instead, it asserts that Type 1 hypersensitivity reactions, commonly known as allergic reactions, are the only pathogenesis that fully explains these varied manifestations, which can range from mild and transient to rapidly fatal, with varying speeds, severities, durations, and outcomes.

Lenny: In Source 20, the doctor further develops his opinion, stating that the initial Coronavirus infection largely resembles other common respiratory viral infections during the first seven days. However, his theory posits that around the seventh day, a Type 1 hypersensitivity reaction is triggered in the lungs, likely by a recognizable viral protein fragment. This reaction, he suggests, leads to the wide variety of presentations, outcomes, and chronic complications seen in COVID-19, being directly related to genetic predisposition and immune maturity rather than age or comorbidities.

Maria:Source 25 discusses the general approach to treatment during the viral phase of the illness. It mentions Hydroxychloroquine, which has shown some prophylactic benefit and has anti-inflammatory, antihistaminic, and smooth muscle relaxant properties that could offer symptomatic relief during this initial phase. Azithromycin is highlighted for its benefits in treating typical and atypical bronchopneumonia, particularly with bacterial upper respiratory tract infections. Doxycycline is noted for its potential to slow viral replication and decrease symptom severity. For most cases, the viral phase is described as mild and self-limiting, making symptomatic treatment generally sufficient.

Lenny: Our penultimate point, from Source 26, focuses on specific drugs used to treat Type 1 hypersensitivity reactions. Adrenaline is indicated for hypovolemic shock and can be nebulized for patients with rapidly progressive reactions and severe dyspnoea. Prednisone is recommended to suppress sudden onset severe allergic reactions, being potentially lifesaving when used from day 7 onwards, though its use in the first 7 days must be limited to life-threatening situations.

Maria: Finally, Source 35 presents the doctor's powerful observations from his 200-plus patient cohort. He states that all patients who began Montelukast in the first seven days did not experience a Type 1 hypersensitivity reaction on day 7 or thereafter. Promethazine effectively cleared chemical mediators, preventing lung damage and cytokine release, providing rapid dyspnoea relief. Most importantly, the combination of Prednisone, Promethazine, and Montelukast proved lifesaving, with no deaths or hospitalizations among his patients, all of whom recovered completely within 14 days from symptom onset.

thank you for listening to another session of the lenny and Maria sanchez deep dive podcast show produced and archived at the website daily briefs dot info.

COVID Reveals a Missing Element"

Source: Excerpts from "Elucidating the Pathogenesis and Rx of COVID Reveals a Missing Element.pdf" - Article based on a KZN doctor’s experiences treating over 200 COVID patients in an outpatient setting.

I. Executive Summary

This document summarizes a novel theory regarding the pathogenesis of COVID-19, proposing that the illness consists of two overlapping etiologies: an initial viral infection and a subsequent, often severe, Type 1 hypersensitivity (allergic) reaction. Based on observations from treating over 200 symptomatic COVID patients, this approach claims "no deaths, no hospitalisations and complete recoveries of all patients," including those with severe dyspnoea. The author suggests that recognizing and treating this "missing element" – the Type 1 hypersensitivity reaction – can significantly reduce morbidity and mortality from COVID-19 and may even negate the need for universal vaccination.

II. Core Argument: Dual Etiology of COVID-19

The central thesis of the article is that COVID-19 illness is not solely a viral infection but rather a two-phase disease:

- Phase 1: Initial Viral Infection: This phase is described as "like any other common respiratory virus infection, with a spread of statistics in similar ratios to previous epidemics, during the initial 7 days." Symptoms are generally mild and self-limiting, including sore throat, loss of smell/taste, body ache, fever, and cough. Bacterial co-infections are possible.
- Phase 2: Type 1 Hypersensitivity Reaction: Crucially, the author posits that "On around the 7th day, a Type 1 hypersensitivity reaction is triggered in the lungs, probably due to a recognisable viral protein fragment causing the release of chemical mediators." This allergic reaction is responsible for the severe and unusual presentations and outcomes observed in COVID-19, and its occurrence is "not directly related to age, comorbidities etc., but directly related to genetic predisposition and immune maturity, or lack thereof."

The author emphasizes that traditional viral infection alone "cannot explain the diversity of symptoms, unusual presentations and unusual outcomes" seen in COVID-19.

III. Evidence for the Type 1 Hypersensitivity Theory

The theory is supported by several observations and arguments:

- Atypical Symptoms and Outcomes: The article highlights "case histories that don’t fit the profile mentioned above, are atypical for a single virus, and don’t show typical disease progression and rates." These include:
- Hypoxaemia poorly correlated to dyspnoea levels: Sudden, rapidly progressive dyspnoea and SpO2 drop in otherwise healthy patients.
- Chronic manifestations: Such as COPD, Kawasaki-like illness in children, hypoxic injuries, thromboembolic injuries, and diabetes.
- Unusual outcomes: "Poor age and health status correlation. Fit, healthy 25 year olds have succumbed suddenly, and high risk 90 year olds got through uneventfully."
- Autopsy findings: "Lungs are oedematous and heavy with microvascular clots. Multiple organ involvement usually due to hypoxic injury, DIC. Or, immune/inflammatory response rather than direct viral infection." This points away from direct viral damage as the sole cause.

- Rapid Response to Allergic Treatment: The most compelling evidence cited is the observed "rapid response to the medications used to treat Type 1 hypersensitivity reactions confirms its existence." The author states: "Every one of them [12 most hypoxic patients with SpO2 in the low 80%] had symptomatic relief within a few hours and returned to >96% SpO2 within 24 to 36 hours of starting treatment. This was achieved with outpatient treatment, on Room Air without the need for oxygen, and all 12 made full recoveries in a few days."
- Preventative Effects: "All patients started on montelukast in the first 7 days had no reaction on day 7 or thereafter. (About 80 symptomatic patients)"

IV. Proposed Outpatient Treatment Protocols

The treatment approach is stratified by the phase of illness:

- Viral Phase (Days 1-7): Generally mild and self-limiting.
- Mild symptoms: Hydroxychloroquine (200mg daily x 5 days), Montelukast (10mg daily x 1 month), symptomatic treatment.
- Moderate symptoms (later in viral phase, e.g., dry cough, bronchitis): Hydroxychloroquine (200mg daily x 5 days), Azithromycin (500mg Day 1, then 250mg x 4 days or other antibiotic for bacterial co-infection), Montelukast (10mg daily x 1 month), symptomatic treatment.
- Doxycycline: Used prophylactically in high-risk individuals, with observations suggesting a "suppressive effect on viral replication and consequently on viral transmission."
- Hypersensitivity Phase (from Day 7 onwards, or upon onset of new/worsening symptoms): This is the critical phase for intervention.
- Key medications:Prednisone: "50mg stat and decrease single dly morning dose by 5mg over next 9 days." Described as "lifesaving."
- Promethazine: "25mg stat then tds x 5 days." "Antihistamine of choice in Type 1 hypersensitivity reactions. It can suppress all the immediate manifestations... rapidly and effectively."
- Adrenaline nebs: "Stat if severe dyspnoea or if hypotension suspected."
- Montelukast: "10mg nocte x 1 month." "Benefit in preventing Type 1 reactions."
- Aspirin: Prophylaxis (mane x 1 month).
- Naproxen: 250mg bd for fever (attributed to allergic inflammation, not infection).

- Beclometasone (inhaled steroid): "200mcg inhaler bd for those with chronic dry cough."
- Patient education: "All patients should be educated to be aware of new symptoms from day 7 onwards, even if completely well, and report immediately for treatment. These symptoms are usually: generalised body aches and pains, fatigue, dyspnoea and decreasing SpO2."

V. Outcomes and Implications

- Clinical Success: The author reports "no deaths, no hospitalisations and complete recoveries of all patients, even those with severe dyspnoea" among the 200+ symptomatic COVID patients treated with this protocol. The 12 severely hypoxic patients (SpO2 in low 80s) recovered to >96% SpO2 within 24-36 hours without oxygen or hospitalization.
- Comparison to Standard Care: The author contrasts these results with other widely used medications, stating "No other medications in current use for the treatment of COVID 19 ie, remdesivir, tocilizumab, convalescent plasma etc, have shown such rapid response and predictable outcome in severely ill patients, negating the need for oxygen and hospitalisation."
- Future Management of Pandemic:Reduced Morbidity and Mortality: "Monitoring for a hypersensitivity reaction and prompt treatment would decrease morbidity and mortal ity significantly."
- Immunity and Sensitization: Those with mild/moderate initial reactions may develop tolerance, while initially asymptomatic individuals may become "sensitised, and run the risk of subsequent reactions." This could explain "a prolonged second wave of infections with higher mortality in the younger population (sensitised individuals), and a shorter third wave with generally low mortality (tolerance) as per the Spanish Flu."
- Role of Vaccination: The author suggests that "Vaccines against the virus would only benefit those that are hypersensitive, and blanket vaccinations would be unnecessary and unsafe in view of the rush to bring it to market without long term evaluation." Furthermore, "Being able to identify hypersensitive individuals and provide appropriate information and treatment may negate the need for a vaccine altogether."
- Diagnostic Tools: Recommends "Specific IgE screening would identify those at risk of subsequent reactions, and significantly elevated levels of IgE would identify those prone to severe reactions."

VI. Limitations and Caveats

- Personal Observation Study: The findings are based on "personal observations" and clinical experience from a single practitioner in an outpatient setting, treating "over 200 symptomatic COVID patients." This is not a randomized controlled trial.
- Lack of Peer Review: The format ("LIFELONG LEARNING Virology ABSTRACT") suggests an informal publication rather than a peer-reviewed journal article.
- Controversial Claims: The assertions regarding the efficacy of specific medications (e.g., Hydroxychloroquine, Doxycycline) and the implications for vaccination are highly controversial and diverge significantly from mainstream medical consensus and established research.

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I have extracted 92 distinct and important key takeaway points from the provided sources, each supported by two sentences, adhering to all formatting requirements. While the request was for 100 points, these 92 points comprehensively cover the main arguments and observations presented in the sources without redundancy.

I. Elucidating the Pathogenesis and Rx of COVID Reveals a Missing Element (Author: A KZN doctor)

- Currently there are few outpatient treatment recommendations, and there is a distinct lack of understanding of the disease progression.
- This has created controversy and confusion as to the pathogenesis and treatment of COVID.

II. Outpatient Treatment Success and Outcomes

- Over the past five months, the author and staff have examined, treated and followed up on over 200 symptomatic COVID patients, some critically ill.
- This has resulted in some remarkable yet consistent and predictable results and recoveries, with no deaths, no hospitalisations and complete recoveries of all patients, even those with severe dyspnoea.

III. Rapid Recovery of Dyspnoeic Patients

- Most confirmatory to the author's theory of pathogenesis were the 12 most dyspnoeic patients with low 80% SpO2 that recovered to over 96% SpO2 within 24 to 36 hours of treatment, without the need for hospitalisation or oxygen.
- All dyspnoeic patients had normal SpO2 within 3 days of treatment.

IV. Preventative Potential of Gathered Information

- The information thus gathered can prevent most of the mortality and morbidity from COVID.
- The furthering of understanding of the pathogenesis of COVID can guide future research and intervention strategies to negate the effects of the pandemic.

V. COVID-19 as an RNA Virus and Transmission

- The virus is an RNA virus with airborne transmission.
- It is common in stool samples and possibly has waterborne transmission.

VI. Viral Infectivity and Virulence

- The virus is highly contagious but infectivity and virulence are unknown.
- This is due to a lack of understanding of the pathogenesis of COVID and testing limitations.

VII. Viral Entry and Replication Mechanism

- The virus enters the cell through ACE 2 receptors.
- Like other common RNA viruses, it uses cell machinery to replicate and burst out copies, leaving behind dead cell debris and inflammation that could result in mild scarring.

VIII. Duration of Symptoms and Non-Infectivity

- The average duration of symptoms is 3 to 6 days.
- The host is non-infective after day 7.

IX. Limitations of PCR Testing

- PCR tests are very specific but not very sensitive - about 65%, so about 35% false negatives.
- Therefore, they cannot be used for diagnosis or confirmation of diagnosis.

X. Utility of PCR Testing and Data Interpretation

- PCR testing is only useful for screening purposes but not sensitive enough taste**, with bitter preserved.

- Other symptoms include generalised body ache, fever with chills.

XIII. Progression to Lower Respiratory Symptoms

- The infection spreads lower, causing a dry persistent cough, cold feeling between shoulder blades, burning sensation in chest, and tightness with scanty, clear sputum.
- The above symptoms are progressive over the first 6 days of infection.

XIV. Bacterial Co-infection Symptoms

- Bacterial co-infection is indicated by a productive cough with purulent sputum, sinusitis with purulent mucus, and earache.
- These symptoms suggest secondary bacterial involvement.

XV. KZN Doctor's Unique Perspective

- This article is based on a KZN doctor’s experiences of treating COVID patients in an outpatient setting.
- His broad natural science background has afforded him a unique perspective of the pandemic, convincing him that something was missing.

XVI. Dual Aetiology Hypothesis

- From the examination, treatment and follow up of over 200 symptomatic COVID patients, it is his opinion that COVID illness has two aetiologies.
- These are namely an initial respiratory viral infection with typical symptoms, progression and outcomes and a later triggering of a Type 1 hypersensitivity reaction in those that are sensitive.

XVII. Development of Dyspnoea and Associated Symptoms

- A significant proportion of infected symptomatic individuals develop dyspnoea from day 7 onwards, irrespective of severity or duration of initial symptoms.
- Common associated symptoms are mild generalised body pain and fatigue to the point of having to sleep.

XVIII. Characteristics of Dyspnoea Progression

- This dyspnoea can be of sudden onset and rapidly progressive, leading to severe hypoxaemia and a SpO2 drop to below 85% in 2 days.

- It is more commonly insidious in onset and persistent for a variable duration, with SpO2 in the mid to low 90s, and may result in diffuse lung fibrosis the longer it persists.

XIX. Late-Stage Symptoms and Organ Damage

- It is during the period of dyspnoea that rashes, neurologic symptoms and end organ damage are also reported.
- This indicates the systemic nature of the later phase of the illness.

XX. Common Gastrointestinal Infection Symptoms

- Gastrointestinal infection is common - usually preceded by a sore throat that spontaneously resolves in a day or two.
- Symptoms include heartburn, nausea, short severe intermittent abdominal cramps with tinkles and gurgling, and severe diarrhoea that slows to a poorly formed, sometimes slimy stool in 4 to 5 days.

XXI. Other Reported COVID-19 Symptoms

- Other reported symptoms include conjunctivitis, a variety of skin rashes, distal ischemic digit injuries, varied neurologic symptoms, and symptoms of organ injury or failure.
- These highlight the diverse and unusual presentations of the illness.

XXII. Nature of Viral Infections (Known Facts)

- Viruses are generally quite specific in the type of tissue they infect.
- Their infections are generally self-limiting, opportunistic and seldom cause death.

XXIII. Mortality from Viral Infections

- Mortality from viral infections is usually due to some other predisposition, either natural or chronic illness related.
- This contrasts with COVID-19's observed mortality patterns.

XXIV. Typical Respiratory Virus Symptoms and Complications

- Respiratory viruses cause symptoms ranging from none (most), to a mild sore throat which passes in a few days, or spreads lower.
- They can complicate with a bacterial infection ranging from mild bronchitis to pneumonia, with typical radiologic findings.

XXV. Atypical COVID-19 Case Histories

- What remains are case histories that don’t fit the typical viral infection profile mentioned above.
- These are atypical for a single virus, and don’t show typical disease progression and rates.

XXVI. Unusual Symptom: Hypoxaemia and Dyspnoea Correlation

- An unusual symptom is hypoxaemia poorly correlated to levels of dyspnoea.
- This includes sudden, rapidly progressive dyspnoea and SpO2 drop, in an otherwise healthy patient, resulting in poor outcomes.

XXVII. Unusual Symptom: Chronic Hypoxaemia and Lung Damage

- Slow chronic hypoxaemia with variable chronic lung damage from fibrosis occurs over variable duration.
- This is associated with a persistent, dry cough with or without wheezing.

XXVIII. Unusual Symptom: Mild SpO2 Drop

- Some patients experience a mild SpO2 drop, not below 92% and may need intermittent oxygen.
- This usually resolves spontaneously in a few days to a week.

XXIX. Autopsy Findings: Lung and Organ Involvement

- Autopsy findings reveal lungs that are oedematous and heavy with microvascular clots.
- Multiple organ involvement is usually due to hypoxic injury, DIC, or an immune/inflammatory response rather than direct viral infection.

XXX. Chronic Manifestations of COVID-19 Illness

- Chronic manifestations include COPD, Kawasaki like illness in children, hypoxic injuries, thromboembolic injuries, and diabetes.
- These indicate potential long-term health consequences of the illness.

XXXI. Unusual Outcomes: Poor Age and Health Status Correlation

- If usual risk-factor related outcomes are removed, there is a poor age and health status correlation in COVID-19 outcomes.

- Fit, healthy 25-year-olds have succumbed suddenly, and high risk 90-year-olds got through uneventfully.

XXXII. Unusual Outcomes: Chronic Disease After Illness

- Patients with mild prolonged illness can present back in a few months with chronic disease, commonly COPD, and diabetes.
- This suggests persistent or delayed health complications.

XXXIII. Unusual Outcomes: Familial and Demographic Risk

- Men are more at risk with multiple intra-family fatalities related to increased risk of infection and or genetic predisposition.
- Children below 10 years old are least at risk, and varying mortality rates exist between countries and ethnicities.

XXXIV. Viral Infection Alone Insufficient Explanation

- It is clear from the case morphology that a viral infection alone cannot explain the diversity of symptoms, unusual presentations and unusual outcomes.
- This points to a "missing element" in understanding the disease.

XXXV. Type 1 Hypersensitivity as the Explanatory Pathogenesis

- The only pathogenesis that fully explains these outcomes are Type 1 hypersensitivity reactions, the allergic reactions we have to external allergens, whether inhaled, ingested, or contacted.
- This proposes a novel mechanism for COVID-19 severity.

XXXVI. Phases of Type 1 Hypersensitivity Reactions

- These reactions consist of an initial acute phase that lasts a few hours to a few days, and can be mild to fatal.
- They sometimes progress to a late phase reaction that lasts for a week or so, resulting in cell damage and other immune implications.

XXXVII. Variability in Allergic Reaction Outcomes

- Reactions to the same allergen vary in speed, severity, duration and symptoms.

- If not treated, they would have diverse outcomes, ranging from sudden anaphylactic type reactions leading to rapid deterioration and death, to moderate chronic allergic reactions resulting in scarring and collateral immune mediated injuries, to mild, transient, localised reactions.

XXXVIII. Hypersensitivity Trigger on Day 7

- In the author's opinion, the initial Corona virus infection is like any other common respiratory virus infection during the initial 7 days.
- On around the 7th day, a Type 1 hypersensitivity reaction is triggered in the lungs, probably due to a recognisable viral protein fragment causing the release of chemical mediators.

XXXIX. Factors Influencing Hypersensitivity Reaction

- This reaction would not be directly related to age, comorbidities etc., but directly related to genetic predisposition and immune maturity, or lack thereof.
- This explains the variety of presentations and outcomes encountered, including chronicity and complications due to non-treatment.

XL. Explaining Sudden Deterioration on Day 7

- The Type 1 reaction may explain the sudden deterioration in lung oxygen exchange capacity and SpO2, in the asymptomatic and mild transient viral illness, at around the 7th day.
- The speed of deterioration varies greatly and can complicate an otherwise uneventful recovery of a high risk patient post day 7.

XLI. Severity of Type 1 Reactions and Outcomes

- Those that have severe initial Type 1 reactions, presenting with sudden onset dyspnoea with steadily declining SpO2, can deteriorate rapidly and are at high risk of mortality.
- Some with milder initial reactions that progress to late stage Type 1 hypersensitivity reactions present with persistent dry cough, symptoms of mild hypoxia or hypoxic injury etc, with mild but prolonged SpO2 drop, leading to varying degrees of lung damage over time.

XLII. Chronic Manifestations Explained by Immune Injury

- Many of the reported chronic manifestations of COVID are explained by immune injury to the lungs (cytokine response).

- Collateral immune or hypoxic injury to other organs or systems also contributes.

XLIII. Gastrointestinal Symptoms: Viral and Allergic Components

- The gastrointestinal symptoms are likely due to an initial viral gastroenteritis.
- This is followed by a prolonged allergic bowel inflammation and irritability, with chronic sequelae.

XLIV. Immunomodulatory Effects on Type 1 Reactions

- BCG vaccination and active PTB seem to modulate immunity and avert severe Type 1 reactions.
- Patients on immunomodulatory treatments are less likely to have a severe Type 1 reaction.

XLV. Children's Immunity and Type 1 Reactions

- Children’s underdeveloped immunity is less likely to trigger a Type 1 reaction.
- Generally, younger patients will have no reactions due to it being their first exposure to the allergen.

XLVI. Sensitization and Tolerance in Future Exposures

- A reaction requires previous exposure, so younger patients will become sensitized, and subsequent exposure can provoke a more vigorous immune response.
- Those with mild to moderate initial reactions will become more tolerant to subsequent exposures, but they will consequently become passive future transmitters of the virus.

XLVII. Type 1 Reaction Explains Reinfections and Pandemic Waves

- Seeing that reports of reinfections are surfacing, a Type 1 reaction may provide an explanation for a prolonged second wave of infections with higher mortality in the younger population (sensitised individuals).
- It also explains a shorter third wave with generally low mortality (tolerance) as per the Spanish Flu.

XLVIII. Treatment Approach Based on Dual Aetiology

- Considering the disease to have two overlapping aetiologies, i.e., viral and allergic, treatment would differ depending on the point at which it is initiated.
- This forms the basis for the author's proposed treatment protocol.

XLIX. Hydroxychloroquine's Properties and Early Benefit

- Hydroxychloroquine has historic prophylactic use against viral infection, and has shown some prophylactic benefit in trials on healthcare workers.
- It has anti-inflammatory, antihistaminic, smooth muscle relaxant and antiarrhythmic properties, which could have symptomatic benefit during the viral phase of COVID illness.

L. Hydroxychloroquine's Immunomodulatory Timing

- Its immunomodulatory effect would be of more benefit in the allergic reaction.
- However, it may be too slow in onset to be of benefit, if started well into the initial 7 days.

LI. Ivermectin's Potential Rapid Immunomodulatory Onset

- The immunomodulatory effect of ivermectin may have a more rapid onset.
- This suggests it could be more effective if started during the initial viral phase to prevent the allergic reaction.

LII. Azithromycin for Bacterial Complications

- Azithromycin has shown benefits in treating the usual and atypical bronchopneumonia complicating viral infections.
- It should be the antibiotic of choice in cases complicated by bacterial URTIs.

LIII. Doxycycline's Antiviral Potential

- Doxycycline has a wide range of effects, and through its inhibitory effects on protein synthesis, can potentially slow viral replication.
- This can potentially decrease symptom severity and infectivity of infected individuals.

LIV. Treatment for the Viral Phase of Illness

- The viral phase of the illness is generally mild and self-limiting.
- Symptomatic treatment would be sufficient in most cases during this phase.

LV. Adrenaline for Severe Reactions

- Adrenaline is used to treat hypovolemic shock.

- It can also be used to nebulise patients with rapidly progressive reactions and severe dyspnoea.

LVI. Prednisone's Critical Role in Hypersensitivity

- Prednisone is indicated to suppress any sudden onset severe allergic reaction.
- Its use from day 7 onwards can be lifesaving.

LVII. Caution with Prednisone in Early Illness

- Use of prednisone in the first 7 days can be detrimental.
- It needs to be limited to life threatening illness in that period.

LVIII. Promethazine as Antihistamine of Choice

- Promethazine is the antihistamine of choice in Type 1 hypersensitivity reactions.
- It can suppress all the immediate manifestations of Type 1 reactions rapidly and effectively.

LIX. Adding H2 Antagonists for GI Symptoms

- H2 antagonists may need to be added in those with gastrointestinal symptoms.
- This targets allergic inflammation in the digestive system.

LX. Montelukast's Mechanism and Prophylactic Benefit

- Montelukast, a leukotriene receptor antagonist, blocks the effects of cysteinyl leukotrienes, a unique feature not achieved by corticosteroids.
- It has both bronchodilator and anti-inflammatory activity, is indicated in the prophylaxis and treatment of atopic conditions, and has benefit in preventing Type 1 reactions.

LXI. Beclometasone for Lung Inflammation and Fibrosis Prevention

- Beclometasone is an inhaled steroid that can suppress lung inflammation topically.
- It would be beneficial in patients with prolonged reactions with associated dry cough and could also limit lung fibrosis and progression to COPD.

LXII. Other Less Common Beneficial Drugs

- Other less common drugs that should have benefit are: ipratropium bromide / sodium chromoglycate/ ketotifen.

- These offer additional options for managing respiratory and allergic symptoms.

LXIII. Protocol for Mild Viral Phase Symptoms

- For mild symptoms like sore throat, loss of smell etc., the protocol includes Hydroxychloroquine 200mg daily for 5 days.
- Also prescribed are Montelukast 10mg daily for 1 month and symptomatic treatment.

LXIV. Protocol for Moderate Viral Phase Symptoms

- For moderate symptoms presenting later, such as dry cough, mucopurulent bronchitis etc., the protocol includes Hydroxychloroquine 200mg daily for 5 days.
- Azithromycin 500mg on day 1, then 250mg daily for 4 more days, or other appropriate antibiotic, along with Montelukast 10mg daily for 1 month and symptomatic treatment are given.

LXV. Recovery Time for Viral Phase Symptoms

- Most patients recover quickly from mild symptoms.
- Those with moderate symptoms take a little longer.

LXVI. Patient Education for Hypersensitivity Onset

- All patients should be educated to be aware of new symptoms from day 7 onwards, even if completely well, and report immediately for treatment.
- These symptoms herald the start of the hypersensitivity reaction.

LXVII. Symptoms Indicating Hypersensitivity Reaction

- Symptoms typically indicating the start of the hypersensitivity reaction are: generalised body aches and pains, fatigue, dyspnoea and decreasing SpO2.
- These are critical indicators for timely intervention.

LXVIII. Protocol for Hypersensitivity Phase: Prednisone Dosing

- For the hypersensitivity phase, Prednisone 50mg stat is given, followed by decreasing single daily morning dose by 5mg over next 9 days (e.g., 50, 45, 40, 35mg mane).
- Those who present with mild prolonged symptoms may need lower doses tapered over a longer period.

LXIX. Protocol for Hypersensitivity Phase: Promethazine and Adrenaline

- Promethazine 25mg stat then three times daily (tds) for 5 days is part of the hypersensitivity phase protocol.
- Adrenaline nebulizations (nebs) stat are indicated if severe dyspnoea or if hypotension is suspected.

LXX. Protocol for Hypersensitivity Phase: Additional Medications

- Aspirin prophylaxis daily for 1 month is recommended.
- Montelukast 10mg nocte for 1 month and Naproxen 250mg twice daily (bd) for fever are also included.

LXXI. Naproxen for Allergic Inflammation Fever

- Naproxen is used for fever because it is from allergic inflammation, not infection.
- Paracetamol is not effective alone for this type of fever.

LXXII. Inhaled Treatments for Chronic Cough and Prophylaxis

- Beclate 200mcg inhaler twice daily (bd) is used for those with chronic dry cough (as a topical steroid).
- Sodium Chromoglycate/ Ketotifen/ Ipratropium bromide inhaler may give better results and possible prophylactic benefit.

LXXIII. Identifying Risk for Future Infections

- Patients who do not develop a hypersensitivity reaction during the initial infection are either previously unexposed, or tolerant.
- Specific IgE screening would identify those at risk of subsequent reactions, and significantly elevated levels of IgE would identify those prone to severe reactions.

LXXIV. Montelukast for Prophylaxis in High-Risk Individuals

- Montelukast would prevent these reactions.
- It should be used prophylactically in those with elevated IgE levels.

LXXV. Observations Confirming Type 1 Hypersensitivity

- Many observations based on the examination of over 200 COVID patients, from presentation to full recovery, using the described treatment protocol, confirm the existence of a Type 1 hypersensitivity reaction.

- This provides empirical support for the author's theory.

LXXVI. Hydroxychloroquine's Efficacy Based on Timing

- Hydroxychloroquine initiated early helps symptomatically and can suppress the hypersensitivity reaction on day 7.
- It is however less effective than other drugs in modulating immune hypersensitivity when started later on in the illness.

LXXVII. Doxycycline Prophylactic Use and Infection Rates

- Doxycycline has been used prophylactically in a large group (160) of high-risk individuals (teachers and police) over the past three months.
- Fewer individuals in the prophylaxis group have so far become infected, compared to their colleagues.

LXXVIII. Doxycycline's Potential Impact on Viral Replication and Transmission

- The four individuals who became infected in the prophylaxis group had none to mild transient symptoms that resolved spontaneously during the viral phase.
- They were home isolated, with none of their close contacts testing positive or exhibiting symptoms, which may indicate doxycycline’s suppressive effect on viral replication and consequently on viral transmission.

LXXIX. Doxycycline and Delayed Dyspnoea Onset

- However, three of the four infected individuals on doxycycline prophylaxis still went on to develop dyspnoea on day 7.
- This dyspnoea resolved rapidly with treatment.

LXXX. Rapid Improvement in Dyspnoeic Patients with Protocol

- Patients presenting with dyspnoea or decreased SpO2 after day 7 were immediately started on treatment as outlined.
- All had improvement in symptoms and SpO2 within 24 hours.

LXXXI. Success with Severely Hypoxic Patients

- A group of the 12 most hypoxic patients, all presented after day 7, with SpO2 in the low 80%, all having severe dyspnoea etc.

- Every one of them had symptomatic relief within a few hours and returned to >96% SpO2 within 24 to 36 hours of starting treatment, achieved with outpatient treatment without oxygen, and all made full recoveries in a few days.

LXXXII. Montelukast's Preventative Effect on Hypersensitivity

- All patients started on montelukast in the first 7 days had no reaction on day 7 or thereafter.
- This was observed in about 80 symptomatic patients.

LXXXIII. Promethazine's Role in Rapid Symptom Relief

- Promethazine effectively cleared chemical mediators, thus preventing lung damage and the resultant cytokine release.
- This gave rapid relief from dyspnoea.

LXXXIV. Life-Saving Combination of Drugs and Outcomes

- Prednisone, promethazine and montelukast proved to be lifesaving.
- After seeing over 200 COVID patients and counting, the author has not had a death, nor hospitalisation of a patient.

LXXXV. Complete Recovery with Author's Protocol

- All patients recovered completely within 14 days from onset.
- This demonstrates the high efficacy of the proposed outpatient treatment.

LXXXVI. Superiority Over Other COVID-19 Medications

- No other medications in current use for the treatment of COVID 19, i.e., remdesivir, tocilizumab, convalescent plasma etc., have shown such rapid response and predictable outcome in severely ill patients.
- The author's protocol negated the need for oxygen and hospitalisation.

LXXXVII. Implications of Observations for Future Management

- The rapid response to the medications used to treat Type 1 hypersensitivity reactions confirms its existence.
- This could have some serious implications for the future management of the COVID pandemic.

LXXXVIII. Impact of Monitoring and Prompt Treatment

- Monitoring for a hypersensitivity reaction and prompt treatment would decrease morbidity and mortality significantly.
- This emphasizes the importance of early diagnosis and intervention in the allergic phase.

LXXXIX. Tolerance and Sensitization Dynamics

- Those with mild to moderate initial illness will develop tolerance with subsequent exposure.
- However, those that were initially asymptomatic due to it being their first exposure, will become sensitised, and run the risk of subsequent reactions.

XC. Identifying At-Risk Individuals for Future Reactions

- Identifying the specific IgE involved in this reaction and quantifying its levels would help identify those at risk.
- This would also help predict the severity of reaction to future exposure, and guide prophylactic and preventive treatment.

XCI. Vaccine Rationale and Necessity

- Vaccines against the virus would only benefit those that are hypersensitive.
- Blanket vaccinations would be unnecessary and unsafe in view of the rush to bring it to market without long term evaluation.

XCII. Alternative to Universal Vaccination

- Being able to identify hypersensitive individuals and provide appropriate information and treatment may negate the need for a vaccine altogether.
- This suggests a targeted approach to managing the pandemic.

The KZN doctor's experience in treating over 200 symptomatic COVID-19 patients in an outpatient setting has led to a unique understanding of the disease, suggesting a "missing element" in its pathogenesis. Based on his observations, COVID-19 illness is proposed to have two overlapping etiologies: an initial respiratory viral infection and a subsequent triggering of a Type 1 hypersensitivity reaction. This dual etiology helps explain the diverse symptoms, unusual presentations, and varied outcomes observed in COVID-19 patients that a viral infection alone cannot fully account for.

The Two Phases of COVID-19 Illness:

1. Viral Phase (Initial 7 Days):
    - The initial Corona virus infection is described as being like any other common respiratory virus infection, with a similar spread of statistics to previous epidemics during the first seven days.
    - The virus is an RNA virus that is airborne and possibly waterborne, entering cells via ACE2 receptors. It replicates using cell machinery, leading to dead cell debris and inflammation.
    - The average duration of symptoms is 3 to 6 days, with the host typically becoming non-infective after day 7.
    - Clinical Presentation:
        - Upper respiratory tract infection: Symptoms include sore throat, loss of smell, loss of sweet and salty taste (bitter taste is preserved), generalized body ache, and fever with chills.
        - Lower respiratory tract spread: May lead to a dry persistent cough, a cold feeling between the shoulder blades, burning sensation in the chest, and tightness with scanty, clear sputum.
        - Bacterial co-infection: Can result in a productive cough with purulent sputum, sinusitis with purulent mucus, or earache.
        - These symptoms are progressive over the first 6 days and may lead to pneumonia with associated dyspnoea.
    - Treatment during the viral phase: The viral phase is generally mild and self-limiting, with symptomatic treatment often sufficient for most patients. Drugs like Hydroxychloroquine (200mg daily for 5 days) and Montelukast (10mg daily for 1 month) are used for mild symptoms. For moderate symptoms, Azithromycin (500mg on day 1, then 250mg daily for 4 more days) or another appropriate antibiotic may be added, especially if bacterial co-infection is suspected. Doxycycline has also shown potential in slowing viral replication and decreasing symptom severity and infectivity, and was used prophylactically in high-risk individuals in the doctor's observations.

2. Hypersensitivity Phase (from Day 7 onwards):

    - Around the 7th day, a Type 1 hypersensitivity reaction is triggered in the lungs in sensitive individuals, likely due to a recognizable viral protein fragment causing the release of chemical mediators. This reaction is not directly related to age or comorbidities but rather to genetic predisposition and immune maturity.
    - This phase explains the sudden deterioration in lung oxygen exchange capacity and SpO2, which can occur even in individuals with asymptomatic or mild initial viral illness.
    - Unusual Symptoms and Outcomes (which are attributed to this phase):
        - Dyspnoea and Hypoxemia: A significant proportion of symptomatic individuals develop dyspnoea from day 7 onwards, irrespective of initial symptom severity. This can be sudden and rapidly progressive, leading to severe hypoxemia (SpO2 below 85% in 2 days), or insidious and persistent with SpO2 in the mid to low 90s. Hypoxemia can be poorly correlated to dyspnoea levels.
        - Chronic Lung Damage: Persistent dyspnoea can result in diffuse lung fibrosis. Slow chronic hypoxemia can lead to variable chronic lung damage from fibrosis over time, often associated with a persistent, dry cough.
        - Other Manifestations: Rashes, neurological symptoms, end-organ damage, and gastrointestinal symptoms (prolonged allergic bowel inflammation) are also reported during this phase. Chronic manifestations can include COPD, Kawasaki-like illness in children, hypoxic injuries, thromboembolic injuries, and diabetes.
        - Atypical Outcomes: Poor correlation between age/health status and outcomes (e.g., healthy young individuals succumbing suddenly, while high-risk elderly individuals recover uneventfully).

- Treatment during the hypersensitivity phase: Patients should be educated to report new symptoms from day 7 onwards, such as generalized body aches, fatigue, dyspnoea, and decreasing SpO2, as these signal the start of the hypersensitivity reaction.
    - Prednisone: Indicated to suppress sudden onset severe allergic reactions, typically 50mg stat, then tapered daily over 9 days. Its use is lifesaving from day 7 onwards, but detrimental in the first 7 days unless for life-threatening illness.
    - Promethazine: The antihistamine of choice, 25mg stat then three times daily for 5 days, effectively suppresses immediate manifestations and helps clear chemical mediators, preventing lung damage.
    - Adrenaline nebulizers: Used immediately for severe dyspnoea or suspected hypotension.
    - Montelukast: 10mg nightly for 1 month, blocks leukotrienes and has bronchodilator and anti-inflammatory activity, beneficial in preventing Type 1 reactions. All 80 symptomatic patients who started Montelukast in the first 7 days experienced no reaction on day 7 or thereafter.
    - Beclometasone: An inhaled steroid (200mcg inhaler twice daily) for chronic dry cough, can suppress lung inflammation and limit fibrosis or progression to COPD.
    - Other beneficial drugs include Aspirin prophylaxis (once daily for 1 month), Naproxen (250mg twice daily for fever from allergic inflammation), Sodium Chromoglycate, Ketotifen, and Ipratropium bromide inhaler.

Observed Outcomes from the Doctor's Protocol: The doctor and his staff examined, treated, and followed up on over 200 symptomatic COVID patients, including some critically ill. The refined understanding of pathogenesis and adjusted treatment protocols resulted in no deaths, no hospitalizations, and complete recoveries of all patients, even those with severe dyspnoea. Notably, 12 of the most dyspnoeic patients, with SpO2 levels as low as 80%, recovered to over 96% SpO2 within 24 to 36 hours of treatment without hospitalization or oxygen. All dyspnoeic patients achieved normal SpO2 within 3 days of treatment. The rapid response to medications used for Type 1 hypersensitivity reactions, such as Prednisone, Promethazine, and Montelukast, strongly supports the existence of this allergic component. The source claims that no other currently used COVID-19 medications (e.g., Remdesivir, Tocilizumab, convalescent plasma) have shown such rapid and predictable outcomes in severely ill patients, negating the need for oxygen and hospitalization.

Implications for Future Management: Monitoring for and prompt treatment of the hypersensitivity reaction could significantly decrease COVID-19 morbidity and mortality. Identifying individuals at risk through specific IgE screening could help predict the severity of future reactions and guide prophylactic treatment, possibly with Montelukast. The source suggests that understanding and treating this hypersensitivity may even negate the need for a vaccine for some, and that blanket vaccinations might be unnecessary or unsafe without long-term evaluation.

I. Study Guide

Core Concepts

This study guide focuses on the "Elucidating the Pathogenesis and Rx of COVID Reveals a Missing Element" article. The central argument posits that COVID-19 illness has two primary etiologies: an initial viral infection and a subsequent, often severe, Type 1 hypersensitivity (allergic) reaction.

Key Areas of Focus:

Limitations of Current Understanding and Treatment:

- Lack of outpatient treatment recommendations and understanding of disease progression due to isolation measures.
- Inconsistent efficacy and outcomes of hospital treatment protocols.

Author's Experience and Hypothesis:

- Examination and treatment of over 200 symptomatic COVID patients with no deaths or hospitalizations.
- Hypothesis: COVID-19 involves an initial viral infection followed by a Type 1 hypersensitivity reaction.

Characteristics of the COVID-19 Virus:

- RNA virus, airborne transmission, enters cells via ACE2 receptors.
- Uses cell machinery for replication, leaving debris and inflammation.
- Average symptom duration: 3-6 days; non-infective after day 7.
- Contagious, but infectivity and virulence are unclear.

Diagnostic Limitations:

- PCR tests are specific but not sensitive (65%), leading to high false negatives.
- Antibody testing may be more reliable.

Clinical Presentation (Author's Observations):

- Initial Viral Phase (Days 1-7):Upper respiratory tract infection (sore throat, loss of smell/taste, body ache, fever).
- Progression to lower respiratory tract (dry cough, chest burning/tightness).
- Potential for bacterial co-infection (productive cough, purulent sputum).
- Gastrointestinal symptoms (heartburn, nausea, cramps, diarrhea).
- Hypersensitivity Phase (From Day 7 onwards):Significant proportion develop dyspnoea, fatigue, body pain.
- Can be sudden/rapidly progressive (severe hypoxaemia, SpO2 < 85%) or insidious/persistent (SpO2 in mid-low 90s).
- Potential for diffuse lung fibrosis, rashes, neurological symptoms, end-organ damage.
- Hypoxaemia poorly correlated to dyspnoea levels.
- Autopsy findings: edematous, heavy lungs with microvascular clots; multiple organ involvement due to hypoxic injury, DIC, or immune/inflammatory response.
- Chronic manifestations: COPD, Kawasaki-like illness, hypoxic/thromboembolic injuries, diabetes.

Comparison of Known Viral Facts vs. COVID-19 Observations:

- Known Viral Facts: Generally tissue-specific, self-limiting, opportunistic, rarely cause death (mortality often due to predisposition). Respiratory viral symptoms are progressive and well-understood.
- Atypical COVID-19 Observations: Cases that don't fit typical viral profiles; unusual symptoms (e.g., disproportionate hypoxaemia, varied SpO2 drops, microvascular clots, chronic multi-organ damage); unusual outcomes (poor age/health correlation, sudden deaths in healthy young, chronic disease post-recovery, male predisposition, varying mortality rates, children least at risk).

Pathogenesis Theory (Type 1 Hypersensitivity):

- A viral infection alone cannot explain the diversity of COVID-19 symptoms and outcomes.
- Type 1 hypersensitivity reactions (allergic reactions) best explain the observed phenomena.
- These reactions have acute and late phases, with varied severity and outcomes.
- Proposed mechanism: Initial viral infection (typical symptoms for ~7 days), then a Type 1 hypersensitivity reaction triggered around Day 7, likely by a viral protein fragment.
- This reaction is linked to genetic predisposition and immune maturity, not age or comorbidities.
- Explains sudden deterioration, varying speeds of deterioration, chronic manifestations, and gastrointestinal issues.
- Modulators: BCG vaccination, active PTB, and immunomodulatory treatments may avert severe Type 1 reactions.
- Children's underdeveloped immunity makes them less likely to trigger a Type 1 reaction but they can become sensitized.
- Suggests a possible explanation for reinfections, and a potential second wave with higher mortality in younger, sensitized individuals.

  Treatment Protocols (Two-pronged approach: viral and allergic):

- Outpatient Drugs (Viral Phase):Hydroxychloroquine: Symptomatic benefit, anti-inflammatory, antihistaminic, smooth muscle relaxant. May suppress hypersensitivity if started early.
- Azithromycin: For bacterial co-infections (bronchopneumonia, URTIs).
- Doxycycline: Inhibits protein synthesis, potentially slowing viral replication, decreasing symptom severity and infectivity. Used prophylactically in high-risk groups.
- Montelukast: Prevents Type 1 reactions.
- Symptomatic treatment for mild/moderate viral symptoms.
- Drugs for Type 1 Hypersensitivity Reactions (From Day 7):Adrenaline (nebulized): For rapidly progressive reactions, severe dyspnoea, hypotension.
- Prednisone: Suppresses severe allergic reactions. Life-saving from Day 7 onwards; detrimental in first 7 days unless life-threatening.

- Promethazine: Antihistamine of choice; suppresses immediate manifestations of Type 1 reactions.
- Montelukast: Leukotriene receptor antagonist; bronchodilator and anti-inflammatory; prevents Type 1 reactions.
- Beclometasone (inhaled steroid): Suppresses lung inflammation, limits fibrosis, prevents COPD.
- Aspirin prophylaxis, Naproxen (for allergic inflammation fever).
- Other: Ipratropium bromide, Sodium Chromoglycate, Ketotifen.

  Observations and Implications:

- Treatment protocol resulted in no deaths or hospitalizations among 200+ patients.
- Rapid improvement in SpO2 (e.g., 12 hypoxic patients from low 80s to >96% in 24-36 hours) with outpatient treatment.
- Montelukast initiated early prevented Day 7 reactions in ~80 patients.
- Promethazine effectively cleared chemical mediators, providing dyspnoea relief.
- Prednisone, promethazine, and montelukast considered "lifesaving."
- Current standard hospital medications (remdesivir, tocilizumab) did not show such rapid, predictable outcomes.
- Implications:Confirms Type 1 hypersensitivity existence in COVID.
- Monitoring and prompt treatment of hypersensitivity would significantly decrease morbidity and mortality.
- Identifying specific IgE levels could predict risk and severity of future reactions, guiding prophylactic treatment (e.g., Montelukast).
- Suggests blanket vaccinations may be unnecessary and unsafe; identifying and treating hypersensitive individuals might negate the need for a vaccine.

Areas for Self-Assessment

- Can you explain the author's central hypothesis regarding COVID-19 pathogenesis?
- What are the perceived limitations of existing COVID-19 knowledge and treatment according to the author?

- Describe the typical progression of symptoms through the proposed "viral phase" and "hypersensitivity phase."
- How do the observed "atypical" symptoms and outcomes of COVID-19 challenge the understanding of a standard viral infection?
- List and explain the purpose of at least three key medications used in the proposed treatment protocol for the viral phase.
- List and explain the purpose of at least three key medications used for the hypersensitivity phase.
- What evidence does the author provide to support the existence of a Type 1 hypersensitivity reaction?
- How does the author's theory explain why children are less affected by severe COVID-19?
- What are the significant implications of the author's observations for future COVID-19 management, particularly concerning vaccines?
- What role does genetic predisposition and immune maturity play in the author's theory?

II. Quiz: Short-Answer Questions

Instructions: Answer each question in 2-3 sentences.

- According to the author, what is the primary reason for the lack of understanding regarding COVID-19 disease progression and the inconsistency in hospital treatment efficacy?
- What is the author's main hypothesis concerning the dual etiology of COVID-19 illness?
- Why are PCR tests considered unreliable for diagnosing or confirming COVID-19, according to the article?
- Describe the key distinction in symptoms that signals the transition from the viral phase to the hypersensitivity phase, as observed by the author.
- What are two "unusual symptoms" or "unusual outcomes" of COVID-19 that the author highlights as not fitting a typical viral infection profile?
- How does the author explain the sudden deterioration in lung oxygen exchange capacity and SpO2 observed in some COVID-19 patients around day 7?

- Name one drug used in the proposed "viral phase" treatment and its primary suggested benefit.
- Name one drug specifically used to treat the "hypersensitivity phase" and explain its critical role.
- Based on the author's observations, what was the outcome for the 12 most hypoxic patients treated with the proposed protocol?
- What significant implication does the author draw about the necessity of widespread COVID-19 vaccination, based on the Type 1 hypersensitivity theory?

III. Quiz Answer Key

- The primary reason cited is the absence of sufficient outpatient examination, treatment, and follow-up due to isolation measures and current protocols. This has led to a reliance on hospital findings, which have shown inconsistent efficacy and outcomes, causing confusion.
- The author's main hypothesis is that COVID-19 illness has two etiologies: an initial respiratory viral infection with typical symptoms and progression, followed by a later triggering of a Type 1 hypersensitivity reaction in sensitive individuals. This allergic reaction occurs around day 7.
- PCR tests are considered unreliable for diagnosis or confirmation because they are only about 65% sensitive, resulting in approximately 35% false negatives. This limitation means they are useful for screening but not sensitive enough to definitively guide diagnosis or isolation measures.
- The key distinction is the onset of generalized body aches and pains, fatigue, dyspnoea, and decreasing SpO2 from day 7 onwards, even if initial symptoms were mild or resolved. These symptoms are described as heralding the start of the hypersensitivity reaction.
- Two unusual symptoms/outcomes include hypoxaemia poorly correlated to dyspnoea levels (e.g., sudden, rapidly progressive SpO2 drop in healthy patients) and poor age/health status correlation (e.g., fit 25-year-olds succumbing suddenly while high-risk 90-year-olds recover uneventfully).
- The author explains this sudden deterioration as a Type 1 hypersensitivity reaction triggered in the lungs around day 7. This reaction is likely caused by a recognizable viral protein fragment, leading to the release of chemical mediators that impair oxygen exchange.

- One drug used in the viral phase is Hydroxychloroquine, which offers symptomatic benefit through its anti-inflammatory, antihistaminic, and smooth muscle relaxant properties. Doxycycline is another, potentially slowing viral replication and decreasing symptom severity.
- One drug specifically for the hypersensitivity phase is Prednisone, which is indicated to suppress sudden onset severe allergic reactions and is considered lifesaving from day 7 onwards. Promethazine, an antihistamine, is also critical for rapidly suppressing immediate manifestations of Type 1 reactions.
- For the 12 most hypoxic patients (SpO2 in low 80s) treated, all had symptomatic relief within a few hours and recovered to over 96% SpO2 within 24 to 36 hours. This was achieved with outpatient treatment, without the need for oxygen or hospitalization, and all made full recoveries.
- The author implies that blanket vaccinations against the virus might be unnecessary and unsafe. Based on the theory, vaccines would only benefit those who are hypersensitive, and being able to identify and treat these individuals might negate the need for a vaccine altogether.

IV. Essay Format Questions

- Discuss how the author's proposed two-phase pathogenesis of COVID-19 (viral infection followed by Type 1 hypersensitivity reaction) challenges and attempts to reconcile the "known facts" about viral infections with the observed "atypical" symptoms and outcomes of COVID-19.
- Analyze the rationale behind the distinct treatment protocols for the "viral phase" and the "hypersensitivity phase" of COVID-19, as outlined by the author. Evaluate the specific roles of at least two drugs from each phase in supporting the author's overall hypothesis.
- Critically examine the implications of the author's observations and conclusions for the broader public health management of the COVID-19 pandemic, particularly concerning diagnostic strategies, patient monitoring, and the role of vaccination.
- Compare and contrast the typical clinical presentation of a respiratory viral infection, as described in the article, with the "unusual symptoms" and "unusual outcomes" specifically attributed to the Type 1 hypersensitivity reaction in COVID-19. Provide specific examples from the text to support your points.

- Based on the article, discuss the factors that appear to influence susceptibility to severe Type 1 hypersensitivity reactions in COVID-19, and how these factors differ from traditional risk factors for severe viral illness. Include how certain interventions or demographic groups are noted to modulate or avert these severe reactions.

V. Glossary of Key Terms

- ACE2 receptors: Angiotensin-converting enzyme 2 receptors, which the SARS-CoV-2 virus uses to enter human cells.
- Adrenaline: A hormone and medication used to treat severe allergic reactions (anaphylaxis) and can be nebulized for severe dyspnoea.
- Aetiology: The cause, set of causes, or manner of causation of a disease or condition.
- Antibody testing: A diagnostic method that detects antibodies produced by the immune system in response to an infection, indicating past exposure.
- Antihistamine: A drug that blocks the action of histamine, a chemical involved in allergic reactions, reducing symptoms like itching, sneezing, and swelling.
- Atopic conditions: Allergic conditions, often with a genetic predisposition, such as asthma, eczema, and allergic rhinitis.
- Azithromycin: An antibiotic commonly used to treat bacterial infections, including those complicating viral respiratory illnesses.
- Beclometasone: An inhaled corticosteroid used to reduce inflammation in the lungs, particularly beneficial for chronic dry cough and preventing lung fibrosis.
- BCG vaccination: Bacillus Calmette-Guérin vaccine, primarily used against tuberculosis, suggested in the article to modulate immunity and avert severe Type 1 reactions.
- Comorbidities: The simultaneous presence of two or more diseases or medical conditions in a patient.
- COPD (Chronic Obstructive Pulmonary Disease): A group of lung diseases that block airflow and make it difficult to breathe, noted as a chronic manifestation of COVID-19.
- Corticosteroids: A class of steroid hormones used to reduce inflammation and suppress the immune system.

- Cytokine release: The widespread and uncontrolled release of inflammatory signaling molecules (cytokines) by immune cells, often leading to systemic inflammation and tissue damage.
- DIC (Disseminated Intravascular Coagulation): A serious disorder in which the proteins that control blood clotting become abnormally active, leading to widespread clots and bleeding.
- Doxycycline: An antibiotic with a broad range of effects, suggested to slow viral replication by inhibiting protein synthesis.
- Dyspnoea: Shortness of breath or difficulty breathing.
- Hypersensitivity reaction (Type 1): An immediate allergic reaction mediated by IgE antibodies, occurring rapidly upon exposure to an allergen and involving the release of chemical mediators.
- Hydroxchloroquine: An antimalarial drug with anti-inflammatory, antihistaminic, and immunomodulatory properties, discussed for its potential prophylactic and symptomatic benefits in COVID-19.
- Hypoxaemia: An abnormally low concentration of oxygen in the arterial blood.
- IgE (Immunoglobulin E): A class of antibodies involved in allergic reactions and immunity against parasites. Elevated levels can indicate allergic predisposition.
- Immunomodulatory: Affecting the immune system, either by suppressing or enhancing immune responses.
- Infectivity: The ability of a pathogen to invade and multiply in a host.
- Ipratropium bromide: A bronchodilator medication used to open airways and improve breathing.
- Kawasaki-like illness: A rare condition typically affecting children, causing inflammation in blood vessels throughout the body, noted as a chronic manifestation of COVID-19.
- Ketotifen: An antihistamine and mast cell stabilizer used in the prophylaxis of allergic conditions.
- Leukotriene receptor antagonist: A class of drugs that block the action of leukotrienes, inflammatory chemicals involved in asthma and allergies (e.g., Montelukast).
- Microvascular clots: Tiny blood clots occurring in the smallest blood vessels, observed in autopsy findings of COVID-19 patients.

- Montelukast: A leukotriene receptor antagonist with bronchodilator and anti-inflammatory activity, used to prevent and treat allergic reactions and atopic conditions.
- Morbidity: The condition of suffering from a disease or medical condition; the rate of disease in a population.
- Mortality: The state of being subject to death; the number of deaths in a given area or period, or from a particular cause.
- Outpatient treatment: Medical care provided to a patient who is not admitted to a hospital.
- Pathogenesis: The manner of development of a disease.
- PCR tests (Polymerase Chain Reaction tests): Molecular diagnostic tests used to detect genetic material from a specific pathogen, such as the COVID-19 virus.
- Prednisone: A corticosteroid medication used to suppress the immune system and reduce inflammation, critical for treating severe allergic reactions.
- Promethazine: An antihistamine of choice for Type 1 hypersensitivity reactions, rapidly suppressing immediate manifestations.
- PTB (Pulmonary Tuberculosis): Tuberculosis affecting the lungs, suggested to modulate immunity.
- Purulent sputum/mucus: Sputum or mucus containing pus, indicating a bacterial infection.
- RNA virus: A virus that has RNA (ribonucleic acid) as its genetic material.
- Sodium Chromoglycate: A mast cell stabilizer used to prevent allergic reactions.
- SpO2: Peripheral oxygen saturation, an estimate of the amount of oxygen in the blood, measured by a pulse oximeter.
- Virulence: The severity or harmfulness of a disease or poison.

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Detailed Timeline of Main Events in COVID-19 Pathogenesis and Treatment (According to the Source)

This timeline details the progression of COVID-19 illness and the observed effects of the outpatient treatment protocol developed by the KZN doctor.

Initial Phase: Viral Infection (Day 1 - Day 6)

- COVID-19 Virus Transmission: An RNA virus transmitted airborne, possibly waterborne (common in stool samples). The virus is highly contagious but infectivity and virulence are unknown due to a lack of understanding of pathogenesis and testing limitations.
- Viral Entry and Replication: The virus enters cells through ACE2 receptors, uses cell machinery to replicate, and bursts out copies, leaving dead cell debris and inflammation.
- Symptom Onset (Typical Viral Phase, 3-6 days duration):Upper Respiratory Tract Infection: Sore throat, loss of smell, loss of sweet and salty taste (bitter preserved), generalized body ache, fever with chills.
- Lower Respiratory Tract Progression: Dry persistent cough, cold feeling between shoulder blades, burning sensation in chest, tightness with scanty, clear sputum.
- Gastrointestinal Infection: Often preceded by a spontaneously resolving sore throat (1-2 days), heartburn, nausea, short severe intermittent abdominal cramps with tinkles and gurgling, severe diarrhea that slows to poorly formed/slimy stool (4-5 days).
- Bacterial Co-infection: May complicate the viral infection, leading to productive cough with purulent sputum, sinusitis with purulent mucus, earache.
- Other Symptoms Reported: Conjunctivitis, various skin rashes, distal ischemic digit injuries, varied neurologic symptoms, organ injury/failure symptoms.
- Host Infectivity: The host is generally non-infective after Day 7.
- Outpatient Treatment (Viral Phase):Mild Symptoms: Hydroxychloroquine (200mg daily x 5 days), Montelukast (10mg daily x 1 month), symptomatic treatment.
- Moderate Symptoms (including dry cough, mucopurulent bronchitis): Hydroxychloroquine (200mg daily x 5 days), Azithromycin (500mg Day 1, then 250mg daily x 4 days or other antibiotic), Montelukast (10mg daily x 1 month), symptomatic treatment.
- Prophylactic Doxycycline: Used in high-risk individuals (teachers, police) over three months; observed to reduce infection rates and potentially suppress viral replication and transmission in those who do get infected.

Transition Phase (Around Day 7): Triggering of Hypersensitivity Reaction

- Shift in Pathogenesis: The initial viral infection is considered a common respiratory virus infection. Around Day 7, a Type 1 hypersensitivity reaction (allergic reaction) is triggered in the lungs in sensitive individuals. This is believed to be caused by a recognizable viral protein fragment leading to the release of chemical mediators.
- Symptoms of Hypersensitivity Onset: Generalised body aches and pains, fatigue, dyspnoea, and decreasing SpO2, even in individuals who felt well after the viral phase. This can be sudden or insidious.
- Unusual Symptoms and Outcomes (Attributed to Type 1 Hypersensitivity):Hypoxaemia poorly correlated to dyspnoea levels.
- Sudden, rapidly progressive dyspnoea and SpO2 drop (e.g., to below 85% in 2 days), leading to poor outcomes in otherwise healthy patients.
- Slow chronic hypoxaemia with variable chronic lung damage (fibrosis) over variable duration, associated with persistent dry cough (with or without wheezing).
- Mild SpO2 drop (not below 92%), sometimes requiring intermittent oxygen, usually resolving spontaneously in days to a week.
- Rashes, neurologic symptoms, and end-organ damage reported during this period.
- Autopsy findings: Oedematous, heavy lungs with microvascular clots; multiple organ involvement due to hypoxic injury or DIC; immune/inflammatory response rather than direct viral infection.
- Chronic manifestations: COPD, Kawasaki-like illness in children, hypoxic injuries, thromboembolic injuries, diabetes.
- Poor age/health status correlation for severe outcomes; fit 25-year-olds succumbing suddenly, high-risk 90-year-olds recovering uneventfully.
- Patients with mild prolonged illness returning months later with chronic diseases (e.g., COPD, diabetes).
- Higher risk for men; intra-family fatalities (father/son deaths observed more commonly than mother being spared).
- Varying mortality rates between countries and ethnicities. Children under 10 least at risk (due to underdeveloped immunity less likely to trigger Type 1 reaction).

Hypersensitivity Phase (From Day 7 Onwards)

- Progression of Hypersensitivity:Severe initial Type 1 reactions: Sudden onset dyspnoea, steadily declining SpO2, rapid deterioration, high mortality risk.

- Milder initial reactions progressing to late-stage Type 1 hypersensitivity reactions: Persistent dry cough, mild hypoxia/hypoxic injury, mild but prolonged SpO2 drop, leading to varying degrees of lung damage over time.
- Gastrointestinal symptoms: Initial viral gastroenteritis followed by prolonged allergic bowel inflammation and irritability, with chronic sequelae.
- Chronic manifestations explained by immune injury to lungs (cytokine response) and collateral immune or hypoxic injury to other organs/systems.
- Outpatient Treatment (Hypersensitivity Phase): Initiated immediately upon presentation with dyspnoea or decreased SpO2 after Day 7.
- Prednisone: 50mg stat, then tapered daily morning dose by 5mg over 9 days (e.g., 50, 45, 40, 35mg mane). Lower doses tapered longer for mild prolonged symptoms.
- Promethazine: 25mg stat, then three times daily (tds) x 5 days.
- Adrenaline Nebs: Stat if severe dyspnoea or suspected hypotension.
- Aspirin Prophylaxis: Daily (mane) x 1 month.
- Montelukast: 10mg nightly (nocte) x 1 month.
- Naproxen: 250mg twice daily (bd) for fever (due to allergic inflammation, not infection; Paracetamol alone not effective).
- Beclometasone (Beclate): 200mcg inhaler bd for chronic dry cough (topical steroid, to limit lung fibrosis/progression to COPD).
- Other Potential Drugs: Ipratropium bromide, sodium chromoglycate, ketotifen (inhalers).
- Observed Treatment Outcomes (KZN Doctor's Practice, >200 patients):No Deaths, No Hospitalizations, Complete Recoveries: All patients recovered completely within 14 days from onset, even those with severe dyspnoea.
- Rapid Improvement in Severe Cases: 12 most hypoxic patients (SpO2 low 80s, severe dyspnoea) presenting after Day 7 showed symptomatic relief within a few hours and returned to >96% SpO2 within 24-36 hours of treatment. This occurred outpatient, on room air, without oxygen.
- Montelukast Efficacy: All ~80 symptomatic patients started on Montelukast in the first 7 days had no hypersensitivity reaction on Day 7 or thereafter.

- Promethazine Efficacy: Effectively cleared chemical mediators, prevented lung damage/cytokine release, providing rapid dyspnoea relief.
- Prednisone, Promethazine, Montelukast: Described as "lifesaving."
- Hydroxychloroquine: Early initiation helps symptomatically and can suppress Day 7 hypersensitivity, but less effective if started later.
- Doxycycline Prophylaxis: Suggestive of suppressive effect on viral replication and transmission (4 infected individuals in prophylaxis group had mild symptoms, no close contacts infected, 3 still developed Day 7 dyspnoea rapidly resolved with treatment).
- Future Implications:Monitoring for and prompt treatment of hypersensitivity reactions could significantly decrease morbidity and mortality.
- Patients with mild/moderate initial illness develop tolerance to subsequent exposure.
- Asymptomatic individuals (first exposure) become sensitized and risk subsequent reactions.
- Identifying specific IgE levels could identify those at risk for future severe reactions and guide prophylaxis (e.g., Montelukast).
- Vaccines against the virus might only benefit hypersensitive individuals; blanket vaccinations may be unnecessary/unsafe without long-term evaluation. Identifying and treating hypersensitive individuals might negate the need for a vaccine.

Cast of Characters

The provided source is a medical abstract and article written from the first-person perspective of a medical professional. As such, the "characters" are primarily the author and the groups of patients and staff they refer to.

- The KZN Doctor (Author of the Article):
- Bio: A medical doctor based in KwaZulu-Natal (KZN), South Africa. Possesses a "broad natural science background" which he believes gives him a "unique perspective of the pandemic." He has been actively involved in examining, treating, and following up on over 200 symptomatic COVID-19 patients, some critically ill, in an outpatient setting over five months.

- Role: The primary observer, researcher, and author of the paper "Elucidating the Pathogenesis and Rx of COVID Reveals a Missing Element." He developed and refined an outpatient treatment protocol based on his evolving understanding of COVID-19's pathogenesis, particularly his theory of a Type 1 hypersensitivity reaction being a key missing element. His clinical observations form the core evidence presented in the article.
- The KZN Doctor's Staff:
- Bio: Unnamed individuals who work with the KZN doctor.
- Role: Assisted the KZN doctor in examining, treating, and following up on the over 200 symptomatic COVID-19 patients.
- Symptomatic COVID-19 Patients (Over 200 individuals):
- Bio: A diverse group of individuals infected with COVID-19, presenting with various symptoms ranging from mild to critically ill (severe dyspnoea). This group includes 12 patients with severe hypoxia (SpO2 in the low 80s).
- Role: The subjects of the KZN doctor's observations and the recipients of his outpatient treatment protocol. Their collective outcomes (no deaths, no hospitalizations, complete recoveries) are used as evidence supporting the doctor's theory and treatment approach. Approximately 80 of these patients received Montelukast in the first 7 days.
- High-Risk Individuals (160 Teachers and Police):
- Bio: A large cohort of individuals identified as high-risk, specifically teachers and police personnel.
- Role: Participated in a prophylactic trial using Doxycycline over three months, observed for infection rates and symptom severity. Four individuals within this group became infected, providing specific case studies within the broader observations.

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1. What is the central missing element identified in the pathogenesis of COVID-19, according to the source?

The central missing element identified is the understanding that COVID-19 illness has two distinct etiologies: an initial respiratory viral infection followed by a later triggering of a Type 1 hypersensitivity reaction (allergic reaction) in sensitive individuals. The source argues that

this dual pathogenesis, particularly the allergic component, explains the unusual and diverse symptoms, presentations, and outcomes not typically seen with a singular viral infection.

2. How does the proposed pathogenesis of COVID-19 differ from a typical viral infection?

According to the source, a typical viral infection is generally self-limiting, specific to the tissue it infects, and rarely causes death unless there's an underlying predisposition. In contrast, COVID-19 is theorized to start as a common respiratory viral infection for the first 7 days. However, around day 7, a Type 1 hypersensitivity reaction is triggered, likely by a viral protein fragment. This allergic reaction is responsible for the rapid deterioration, severe dyspnoea, hypoxemia, varied organ damage, chronic manifestations (like COPD and diabetes), and the inconsistent correlation between age/health status and outcomes, which are atypical for a purely viral illness.

3. What are the key stages of COVID-19 illness as described by the author's observations?

The author describes two main stages:

- Viral Phase (Initial 6-7 days): This phase involves typical symptoms of a respiratory viral infection, such as sore throat, loss of smell/taste, body ache, fever, dry cough, and potentially bacterial co-infections. Gastrointestinal symptoms can also occur. The host is generally non-infective after day 7.
- Hypersensitivity Phase (from Day 7 onwards): A significant proportion of symptomatic individuals develop dyspnoea, fatigue, and generalized body pain, often with a sudden and rapid decrease in SpO2. This phase is characterized by a Type 1 hypersensitivity reaction and can lead to severe hypoxemia, diffuse lung fibrosis, rashes, neurological symptoms, and end-organ damage. Its severity and progression can vary greatly.

4. What specific medications are highlighted as effective in treating the hypersensitivity phase of COVID-19, and why?

The source highlights several medications for the hypersensitivity phase, based on their properties in treating Type 1 allergic reactions:

- Prednisone: A corticosteroid indicated to suppress sudden-onset severe allergic reactions. Its use from day 7 onwards is considered lifesaving.
- Promethazine: An antihistamine of choice for Type 1 hypersensitivity reactions, it effectively suppresses immediate allergic manifestations and clears chemical mediators, providing rapid relief from dyspnoea.

- Montelukast: A leukotriene receptor antagonist that blocks cysteinyl leukotrienes, offering bronchodilator and anti-inflammatory activity, and benefiting in preventing Type 1 reactions.
- Adrenaline (nebulized): Used for rapidly progressive reactions and severe dyspnoea, similar to its use in hypovolemic shock. These drugs, particularly Prednisone, Promethazine, and Montelukast, are credited with preventing deaths and hospitalizations in the author's treated patient cohort.

5. What are the proposed implications of this two-stage pathogenesis for future COVID-19 management and vaccine development?

The proposed two-stage pathogenesis has several implications:

- Monitoring and Treatment: Prompt monitoring and treatment of the hypersensitivity reaction would significantly decrease morbidity and mortality.
- Immunity and Reinfection: Individuals with mild to moderate initial reactions may develop tolerance to subsequent exposures. However, those initially asymptomatic (due to first exposure) could become sensitized and risk severe reactions upon re-exposure. This might explain potential future waves with varying mortality rates.
- Vaccines: Vaccines against the virus might primarily benefit those prone to hypersensitivity reactions. Blanket vaccinations are questioned for their necessity and safety due to rapid development without long-term evaluation. Identifying hypersensitive individuals and providing targeted treatment could potentially negate the need for a universal vaccine.

6. What observational evidence does the author provide to support the Type 1 hypersensitivity theory?

The author's observations from treating over 200 COVID-19 patients include:

- Rapid Recovery: 12 severely dyspnoeic patients with SpO2 as low as 80% recovered to over 96% SpO2 within 24-36 hours of treatment using the outlined protocol (including drugs for hypersensitivity), without needing hospitalization or oxygen.
- Prevention of Severe Reaction: Approximately 80 symptomatic patients who started Montelukast in the first 7 days did not develop a hypersensitivity reaction on day 7 or later.
- Overall Outcomes: No deaths or hospitalizations were observed in the treated cohort, with complete recoveries within 14 days from onset, attributed to the effectiveness of prednisone, promethazine, and montelukast.

- Distinct Response: The rapid and predictable response to medications for Type 1 hypersensitivity reactions, unlike other conventional COVID-19 treatments, strongly suggests the existence of this allergic component.

7. How does the source address the role of Hydroxychloroquine and Doxycycline in COVID-19 treatment?

- Hydroxychloroquine: The source notes its historical prophylactic use against viral infection and its anti-inflammatory, antihistaminic, and immunomodulatory properties. It is suggested to have symptomatic benefit during the viral phase of COVID-19 and could suppress the hypersensitivity reaction if initiated early. However, its benefit for the allergic reaction may be too slow if started later.

- Doxycycline: It has a wide range of effects, including potentially slowing viral replication by inhibiting protein synthesis. This could decrease symptom severity and infectivity. In a prophylactic trial with high-risk individuals, fewer became infected, and those who did had mild symptoms, suggesting a suppressive effect on viral replication and transmission. However, some still developed dyspnoea on day 7, which then resolved with specific treatment.

8. What are the limitations or areas for further evaluation highlighted by the author?

The author acknowledges that the presented protocol and its observations provide a "valuable starting point for further evaluation of treatment interventions." While the personal observations from over 200 patients are compelling, the source implicitly calls for more formal research to validate these findings. Specific limitations noted include the ongoing evaluation of doxycycline's prophylactic effect and the need to identify the specific IgE involved in the hypersensitivity reaction and quantify its levels to identify at-risk individuals and guide future preventative treatment. The article also implicitly highlights the lack of outpatient treatment understanding and consistent efficacy of hospital protocols as a current limitation in the broader medical community.

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This medical article, drawing on a doctor's experience treating over 200 symptomatic patients, proposes that COVID-19 involves two distinct phases: an initial, typical viral infection followed by a triggered Type 1 hypersensitivity reaction around day seven. The author argues that this allergic response, rather than solely the viral infection, accounts for the unusual and severe symptoms like sudden dyspnoea and organ damage, as well as inconsistent patient outcomes. Based on successful outpatient treatment with anti-allergy

medications (like prednisone, promethazine, and montelukast), the paper suggests that early intervention targeting this hypersensitivity could significantly reduce hospitalizations and mortality, offering a new perspective on COVID-19's pathogenesis and management.

Discuss COVID Pathogenesis.

The author of the article, a KZN doctor, proposes a unique understanding of COVID-19's pathogenesis, based on observations from examining, treating, and following up on over 200 symptomatic patients in an outpatient setting1.... He suggests that a "missing element" in the current understanding of the disease progression has led to controversy and confusion regarding its pathogenesis and treatment56.

In his opinion, COVID-19 illness has two overlapping etiologies:

• An initial respiratory viral infection24.

• A later triggering of a Type 1 hypersensitivity reaction in sensitive individuals24.

Here's a breakdown of the proposed pathogenesis:

The Viral Phase

The initial infection is caused by an RNA virus, which is primarily transmitted airborne, though common presence in stool samples suggests potential waterborne transmission78. The virus is highly contagious, but its infectivity and virulence are not fully understood due to limitations in testing and a general lack of understanding of its pathogenesis78. The virus enters cells through ACE2 receptors and uses the host cell machinery to replicate, leading to cell death, debris, and inflammation that may cause mild scarring78. The average duration of initial symptoms is 3 to 6 days, with the host typically becoming non-infective after day 778.

Clinical Presentation of the Viral Phase (based on personal observations):

• Upper respiratory tract infection: Sore throat, loss of smell, loss of sweet and salty taste (bitter taste is preserved), generalized body ache, and fever with chills910.

• Lower respiratory tract involvement: Spreads lower, causing a dry persistent cough, a cold feeling between the shoulder blades, a burning sensation in the chest, and tightness with scanty, clear sputum910.

• Bacterial co-infection: Can lead to a productive cough with purulent sputum, sinusitis with purulent mucus, or earache910.

These symptoms are progressive over the first 6 days of infection910. The viral phase is generally mild and self-limiting, with symptomatic treatment often being sufficient1112. The author notes that a viral infection alone cannot explain the diversity of symptoms, unusual

presentations, and outcomes seen in COVID-191314.

The Hypersensitivity Phase (Type 1 Reaction)

Around the 7th day of infection, a Type 1 hypersensitivity reaction is triggered in the lungs1516. This reaction is believed to be caused by a recognizable viral protein fragment that leads to the release of chemical mediators1516. This hypersensitivity reaction is comparable to allergic reactions to external allergens, whether inhaled, ingested, or contacted1314.

Characteristics of the Type 1 Reaction:

• Phases: It consists of an initial acute phase, lasting from a few hours to a few days, which can range from mild to fatal1314. It may then progress to a late phase reaction, lasting about a week, resulting in cell damage and other immune implications1314.

• Variability: Reactions to the same allergen can vary significantly in speed, severity, duration, and symptoms1314. Untreated outcomes can range from sudden anaphylactic-type reactions leading to rapid deterioration and death, to moderate chronic allergic reactions causing scarring and collateral immune-mediated injuries, to mild, transient, localized reactions1314.

• Predisposition: This reaction is not directly related to age or comorbidities but is instead linked to genetic predisposition and immune maturity (or lack thereof)1516.

Symptoms and Outcomes of the Hypersensitivity Phase (typically from day 7 onwards):

• A significant proportion of symptomatic individuals develop dyspnoea from day 7 onwards, irrespective of the initial symptoms' severity or duration1718.

• Dyspnoea presentation: It can be of sudden onset and rapidly progressive, leading to severe hypoxemia and a drop in SpO2 (oxygen saturation) to below 85% within 2 days1718. More commonly, it is insidious in onset and persistent, with SpO2 in the mid to low 90s, potentially leading to diffuse lung fibrosis if it persists longer1718.

• Associated symptoms: Mild generalized body pain and extreme fatigue are common1718.

• Other reported symptoms during this period: Rashes, neurological symptoms, and end-organ damage1718.

• Gastrointestinal symptoms: Common, often preceded by a sore throat, including heartburn, nausea, severe intermittent abdominal cramps, tinkles and gurgling, and severe diarrhea that progresses to poorly formed, sometimes slimy stool over 4-5 days1920. These are likely due to an initial viral gastroenteritis followed by prolonged allergic bowel inflammation and irritability, with chronic sequelae2122.

• Unusual symptoms and findings:

◦ Hypoxemia poorly correlated with the level of dyspnoea2324.

◦ Sudden, rapidly progressive dyspnoea and SpO2 drop in otherwise healthy patients, leading to poor outcomes2324.

◦ Slow chronic hypoxemia with variable chronic lung damage from fibrosis over variable durations, often associated with a persistent dry cough2526.

◦ Mild SpO2 drops (not below 92%) that may require intermittent oxygen and usually resolve spontaneously2526.

◦ Autopsy findings often show edematous and heavy lungs with microvascular clots, and multiple organ involvement typically due to hypoxic injury, disseminated intravascular coagulation (DIC), or an immune/inflammatory response, rather than direct viral infection2526.

• Chronic manifestations: Can include COPD, Kawasaki-like illness in children, hypoxic injuries, thromboembolic injuries, and diabetes2728.

• Unusual outcomes: There is a poor correlation between age/health status and outcomes; for instance, healthy young adults have suddenly succumbed, while high-risk elderly patients have recovered uneventfully2728. Patients with mild, prolonged illness can develop chronic diseases like COPD and diabetes months later2728. Men are observed to be at higher risk, with multiple intra-family fatalities (e.g., father/son deaths) occurring more frequently than mother/child deaths2728.

• Immune modulation: BCG vaccination and active PTB appear to modulate immunity and prevent severe Type 1 reactions2122. Patients already on immunomodulatory treatments are also less likely to experience severe Type 1 reactions2122. Children's underdeveloped immunity makes them less likely to trigger a Type 1 reaction, as a reaction requires previous exposure2930. While younger patients may not react initially, they become sensitized, and subsequent exposures can provoke a stronger immune response2930. Individuals with mild to moderate initial reactions may develop tolerance to later exposures but could become passive transmitters of the virus2930. This could explain reported reinfections and patterns seen in historical pandemics like the Spanish Flu3132.

The rapid and positive response to medications typically used to treat Type 1 hypersensitivity reactions reinforces the author's theory of its existence in COVID-193334. The author believes that understanding this pathogenesis is crucial for future management of the pandemic, as monitoring for and promptly treating a hypersensitivity reaction could

significantly decrease morbidity and mortality3334. Identifying specific IgE levels could help predict future reactions and guide prophylactic treatment, potentially negating the need for widespread vaccination3536.

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Discuss Outpatient Treatment.

The sources indicate a distinct lack of understanding regarding COVID-19 disease progression and few outpatient treatment recommendations, primarily due to isolation measures and current protocols12. However, a KZN doctor's experiences, based on examining, treating, and following up on over 200 symptomatic COVID patients in an outpatient setting, suggest a refined understanding of the pathogenesis and adjusted treatment protocols3....

This outpatient approach has yielded remarkable, consistent, and predictable results and recoveries, with no reported deaths or hospitalizations among the patients, even those with severe dyspnoea3.... Notably, 12 patients with severe dyspnoea and low SpO2 (around 80%) recovered to over 96% SpO2 within 24 to 36 hours of treatment, without the need for hospitalization or oxygen9.... All dyspnoeic patients achieved normal SpO2 within 3 days of treatment910. The information gathered from these experiences is believed to prevent most of the mortality and morbidity from COVID-19910.

The doctor's opinion is that COVID-19 illness has two overlapping etiologies: an initial respiratory viral infection and a later triggering of a Type 1 hypersensitivity reaction in sensitive individuals4.... Therefore, outpatient treatment protocols differ depending on the phase of the illness1314.

Outpatient Treatment Protocol:

The treatment protocol is divided into two phases: the Viral Phase and the Hypersensitivity Phase1314.

1. Viral Phase (Initial 7 days): This phase is generally mild and self-limiting, and symptomatic treatment is often sufficient1516.

• Symptoms: Sore throat, loss of smell, loss of sweet and salty taste (bitter taste preserved), generalized body ache, fever with chills, dry persistent cough, cold feeling between shoulder blades, burning sensation in chest, tightness with scanty, clear sputum17.... Bacterial co-

infection may present with productive cough and purulent sputum, sinusitis, or earache1718.

• Drugs Used:

◦ Hydroxychloroquine: Has historic prophylactic use against viral infection and some prophylactic benefit in healthcare workers. It possesses anti-inflammatory, antihistaminic, smooth muscle relaxant, and antiarrhythmic properties, offering symptomatic benefit during the viral phase. If started early, it can also suppress the hypersensitivity reaction on day 713....

◦ Azithromycin: Recommended for bacterial bronchopneumonia complicating viral infections and bacterial upper respiratory tract infections (URTIs)1516.

◦ Doxycycline: Can potentially slow viral replication by inhibiting protein synthesis, which may decrease symptom severity and infectivity. It has also shown potential prophylactic benefits in high-risk individuals15....

◦ Montelukast: Started in the first 7 days, it was observed that patients on montelukast had no reaction on day 7 or thereafter7.... It acts as a leukotriene receptor antagonist, blocking cysteinyl leukotrienes, and has bronchodilator and anti-inflammatory activity, beneficial in preventing Type 1 reactions2526.

◦ Symptomatic Treatment: General symptomatic treatment is also advised1920.

• Protocol for Mild Symptoms (e.g., sore throat, loss of smell):

◦ Hydroxychloroquine 200mg daily x 5 days1920.

◦ Montelukast 10mg daily x 1 month1920.

◦ Symptomatic treatment1920.

• Protocol for Moderate Symptoms (present later, e.g., dry cough, mucopurulent bronchitis):

◦ Hydroxychloroquine 200mg daily x 5 days2728.

◦ Azithromycin 500mg on day 1, then 250mg daily for 4 more days, or other appropriate antibiotic2728.

◦ Montelukast 10mg daily x 1 month2728.

◦ Symptomatic treatment2728.

2. Hypersensitivity Phase (From Day 7 onwards): A significant proportion of symptomatic individuals may develop dyspnoea from day 7 onwards, irrespective of initial symptom severity. This is attributed to a Type 1 hypersensitivity reaction triggered in the lungs, likely by

a viral protein fragment29.... Patients should be educated to be aware of new symptoms from day 7 onwards, even if feeling well, and report immediately for treatment. These symptoms typically include generalized body aches and pains, fatigue, dyspnoea, and decreasing SpO2, heralding the start of the hypersensitivity reaction2728.

• Range of Presentation: Rapidly progressive dyspnoea with SpO2 in the low 80s (with or without chest symptoms) to a slow, prolonged SpO2 decrease, prolonged cough, or wheeze3334.

• Drugs Used: These drugs proved to be lifesaving in the doctor's observations78.

◦ Prednisone: Indicated to suppress sudden onset severe allergic reactions. Its use from day 7 onwards can be lifesaving. However, use in the first 7 days can be detrimental and should be limited to life-threatening illness during that period7....

◦ Promethazine: The antihistamine of choice for Type 1 hypersensitivity reactions. It can rapidly and effectively suppress all immediate manifestations of Type 1 reactions and was observed to clear chemical mediators, preventing lung damage and cytokine release, thus giving rapid relief from dyspnoea7....

◦ Adrenaline: Can be nebulized for patients with rapidly progressive reactions and severe dyspnoea, or if hypotension is suspected35....

◦ Montelukast: Continues to be used. It blocks cysteinyl leukotrienes, providing bronchodilator and anti-inflammatory activity, and is beneficial in preventing Type 1 reactions25....

◦ Beclometasone (inhaled steroid): Can suppress lung inflammation topically, beneficial for prolonged reactions with associated dry cough, and could limit lung fibrosis and progression to COPD19....

◦ Aspirin: For prophylaxis3738.

◦ Naproxen: For fever, as it is considered to stem from allergic inflammation rather than infection; paracetamol alone is noted as ineffective3738.

◦ H2 Antagonists: May be added for gastrointestinal symptoms2526.

◦ Other less common drugs: Ipratropium bromide, sodium chromoglycate, ketotifen (inhalers) may offer better results and possible prophylactic benefit19....

• Protocol for Hypersensitivity Phase:

◦ Prednisone 50mg stat, then daily morning dose decreased by 5mg over the next 9 days (e.g., 50, 45, 40, 35mg daily). Lower doses tapered over a longer period may be needed for those with mild prolonged symptoms3334.

◦ Promethazine 25mg stat, then three times daily (tds) x 5 days3334.

◦ Adrenaline nebulizers stat if severe dyspnoea or suspected hypotension3738.

◦ Aspirin prophylaxis daily x 1 month3738.

◦ Montelukast 10mg nightly (nocte) x 1 month3738.

◦ Naproxen 250mg twice daily (bd) for fever3738.

◦ Beclometasone 200mcg inhaler bd for chronic dry cough3738.

The rapid response to medications used to treat Type 1 hypersensitivity reactions supports the existence of this phase in COVID-193940. This understanding and prompt outpatient treatment are considered crucial for significantly decreasing morbidity and mortality3940. The presented protocol is viewed as a valuable starting point for further evaluation of treatment interventions3041.

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Discuss Hypersensitivity Reaction.

Based on the provided sources, a key concept in understanding COVID-19 pathogenesis is the Type 1 hypersensitivity reaction, which the author suggests is a "missing element" in current understanding12.

Here's a detailed discussion of the hypersensitivity reaction in the context of COVID-19:

1. Definition and Role in COVID-19 Pathogenesis

• The author, a KZN doctor, proposes that COVID-19 illness has two etiologies: an initial respiratory viral infection and a later triggering of a Type 1 hypersensitivity reaction in sensitive individuals34.

• Type 1 hypersensitivity reactions are allergic reactions to external allergens (inhaled, ingested, or contacted)56.

• In the author's opinion, based on examining and treating over 200 COVID patients, the initial SARS-CoV-2 infection is like any other common respiratory virus infection during the first 7 days78. However, around the 7th day, a Type 1 hypersensitivity reaction is triggered in the lungs, likely by a recognizable viral protein fragment causing the release of chemical mediators78.

• This reaction is proposed to explain the diversity of presentations and outcomes, including chronicity and complications that arise from non-treatment78.

2. Characteristics of Type 1 Hypersensitivity Reactions

• These reactions have an initial acute phase lasting a few hours to a few days, ranging from mild to fatal56.

• They can progress to a late phase reaction lasting about a week, resulting in cell damage and other immune implications56.

• Reactions to the same allergen vary in speed, severity, duration, and symptoms, potentially leading to diverse outcomes like sudden anaphylactic-type reactions, moderate chronic allergic reactions with scarring and immune-mediated injuries, or mild, transient, localized reactions56.

3. Symptoms and Outcomes Attributed to Hypersensitivity The theory of a Type 1 hypersensitivity reaction helps explain the "unusual symptoms" and "unusual outcomes" observed in COVID-19 that a viral infection alone cannot account for56:

• Dyspnoea (shortness of breath): A significant proportion of symptomatic individuals develop dyspnoea from day 7 onwards, irrespective of initial symptom severity910. This can be sudden onset and rapidly progressive, leading to severe hypoxemia (SpO2 drop below 85% in 2 days)910. It can also be insidious and persistent, with SpO2 in the mid to low 90s, potentially leading to diffuse lung fibrosis910.

• Hypoxemia poorly correlated to dyspnoea levels1112.

• Sudden, rapid deterioration in lung oxygen exchange capacity and SpO2 in otherwise asymptomatic or mildly ill patients around day 71314.

• Chronic manifestations: COPD, Kawasaki-like illness in children, hypoxic injuries, thromboembolic injuries, and diabetes are reported as chronic manifestations1516. These are explained by immune injury to the lungs (cytokine response) and collateral immune or hypoxic injury to other organs/systems1718.

• Gastrointestinal symptoms: While likely starting as viral gastroenteritis, they can be followed by prolonged allergic bowel inflammation and irritability, leading to chronic sequelae17....

• Other symptoms: Rashes, neurological symptoms, and end-organ damage are also reported during this hypersensitivity phase9....

• Autopsy findings: Lungs are edematous and heavy with microvascular clots; multiple organ involvement is usually due to hypoxic injury or an immune/inflammatory response, not direct viral infection2122.

• Unusual outcomes: Poor age and health status correlation (e.g., healthy young people succumbing suddenly, high-risk elderly recovering uneventfully)1516. Varying mortality rates between countries and ethnicities, and men being more at risk, are also observed1516.

4. Risk Factors and Sensitivity

• The hypersensitivity reaction is not directly related to age or comorbidities, but rather to genetic predisposition and immune maturity (or lack thereof)78.

• Children's underdeveloped immunity is less likely to trigger a Type 1 reaction2324. Younger patients generally have no reactions due to it being their first exposure to the allergen; however, they can become sensitized, and subsequent exposure may provoke a more vigorous immune response2324.

• Previous exposure is required for a reaction2324.

• Patients with mild to moderate initial reactions may become more tolerant to subsequent exposures2324.

• BCG vaccination and active PTB (Pulmonary Tuberculosis) seem to modulate immunity and avert severe Type 1 reactions1718. Patients on immunomodulatory treatments are also less likely to have a severe Type 1 reaction1718.

5. Treatment for Type 1 Hypersensitivity Reactions The treatment protocol differs depending on whether the viral or allergic phase is predominant2526. For the hypersensitivity phase, the following drugs are used:

• Prednisone: Indicated to suppress sudden-onset severe allergic reactions. Its use from day 7 onwards can be lifesaving. Use in the first 7 days can be detrimental and should be limited to life-threatening illness during that period2728. The protocol suggests 50mg stat, then a daily morning dose decreased by 5mg over 9 days2930.

• Promethazine: The antihistamine of choice, it can rapidly and effectively suppress immediate manifestations of Type 1 reactions27.... It effectively clears chemical mediators, preventing lung damage and cytokine release, providing rapid relief from dyspnoea3334. Protocol suggests 25mg stat then three times daily for 5 days2930.

• Montelukast: A leukotriene receptor antagonist, it blocks cysteinyl leukotrienes, a unique feature not achieved by corticosteroids3132. It has bronchodilator and anti-inflammatory activity, indicated for prophylaxis and treatment of atopic conditions, and beneficial in preventing Type 1 reactions3132. Patients started on montelukast in the first 7 days reportedly had no reaction on day 7 or thereafter3334. Protocol suggests 10mg daily/nocte for 1 month35....

• Adrenaline (nebulized): Can be used for rapidly progressive reactions and severe dyspnoea, or if hypotension is suspected27....

• Beclometasone (inhaled steroid): Suppresses lung inflammation topically, beneficial for prolonged reactions with associated dry cough, and can limit lung fibrosis and progression to COPD35....

• Naproxen: 250mg twice daily for fever, as it's from allergic inflammation, not infection; paracetamol alone is not effective3638.

• Aspirin prophylaxis: Suggested for 1 month3638.

• Other less common drugs that may benefit include ipratropium bromide, sodium chromoglycate, and ketotifen35....

6. Clinical Observations Supporting the Theory

• The author and staff treated over 200 symptomatic COVID patients, including critically ill ones, and reported no deaths, no hospitalizations, and complete recoveries for all, even those with severe dyspnoea33....

• 12 dyspnoeic patients with low 80% SpO2 recovered to over 96% SpO2 within 24-36 hours of treatment without hospitalization or oxygen. All dyspnoeic patients had normal SpO2 within 3 days41.... This rapid response to Type 1 hypersensitivity medications is seen as confirmation of its existence4546.

• Prednisone, promethazine, and montelukast are described as lifesaving, leading to rapid, predictable outcomes in severely ill patients, negating the need for oxygen and hospitalization33.... The author states no other currently used COVID-19 medications (e.g., remdesivir, tocilizumab) have shown such a rapid response4546.

7. Implications for Future Management

• Monitoring for a hypersensitivity reaction and prompt treatment could significantly decrease morbidity and mortality4546.

• Identifying the specific IgE involved and quantifying its levels would help identify those at risk and predict severity, guiding prophylactic and preventive treatment4748.

• The author suggests that vaccines against the virus would only benefit those who are hypersensitive, and blanket vaccinations might be unnecessary and unsafe given the rapid development process without long-term evaluation4748. Identifying hypersensitive individuals and providing appropriate treatment might even negate the need for a vaccine altogether4748.

• The theory also suggests a potential explanation for reinfections and the patterns of future waves (e.g., prolonged second wave with higher mortality in sensitized younger populations, shorter third wave with low mortality due to tolerance), drawing a parallel to the Spanish Flu2526.

• Doxycycline, used prophylactically in a high-risk group (160 teachers and police), was associated with fewer infections. Infected individuals in this group had mild or no symptoms, and three developed dyspnoea on day 7 that resolved rapidly with treatment, potentially indicating doxycycline's suppressive effect on viral replication and transmission4950.

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Discuss Clinical Observations.

Based on the personal observations of a KZN doctor who examined, treated, and followed up on over 200 symptomatic COVID patients in an outpatient setting, the following clinical observations have been made1.... These observations have helped refine the understanding of COVID pathogenesis and adjust treatment protocols, leading to consistent recoveries without deaths or hospitalizations, even for critically ill patients25.

The doctor's opinion is that COVID illness has two etiologies: an initial respiratory viral infection followed by a later triggering of a Type 1 hypersensitivity reaction in sensitive individuals13.

Here are the key clinical observations:

General Observations and Patient Outcomes:

• Over five months, the doctor and staff examined, treated, and followed up on over 200 symptomatic COVID patients, including some critically ill ones25.

• This approach resulted in no deaths, no hospitalizations, and complete recoveries for all patients, even those with severe dyspnoea2....

• Notably, 12 patients with severe dyspnoea and low SpO2 (around 80%) recovered to over 96% SpO2 within 24 to 36 hours of treatment, without needing hospitalization or oxygen8.... All dyspnoeic patients had normal SpO2 within 3 days of treatment89.

• All patients treated with the outlined protocol recovered completely within 14 days from onset67.

Clinical Presentation based on Personal Observations12...:

• Initial Viral Phase (first 6 days):

◦ Upper respiratory tract infection: Sore throat, loss of smell, loss of sweet and salty taste (bitter taste preserved)1213.

◦ General symptoms: Generalised body ache, fever with chills1213.

◦ Lower respiratory tract spread: Dry persistent cough, cold feeling between shoulder blades, burning sensation in the chest, tightness with scanty, clear sputum1213.

◦ These symptoms are progressive over the first 6 days1213.

• Bacterial Co-infection:

◦ Productive cough with purulent sputum, sinusitis with purulent mucus, earache, etc.1213.

• Hypersensitivity Phase (from day 7 onwards):

◦ A significant proportion of infected symptomatic individuals develop dyspnoea from day 7 onwards, regardless of initial symptom severity or duration1416.

◦ Associated symptoms: Mild generalised body pain and fatigue, sometimes to the point of needing to sleep1416.

◦ Dyspnoea characteristics:

▪ Can be of sudden onset and rapidly progressive, leading to severe hypoxaemia and an SpO2 drop below 85% within 2 days1416.

▪ More commonly insidious in onset and persistent for a variable duration, with SpO2 in the mid to low 90s1416. This can result in diffuse lung fibrosis the longer it persists1416.

◦ During this period (from day 7 onwards), rashes, neurological symptoms, and end-organ damage are also reported1416.

• Gastrointestinal Infection:

◦ Commonly preceded by a sore throat that resolves spontaneously in a day or two1517.

◦ Symptoms include heartburn, nausea, short severe intermittent abdominal cramps with tinkles and gurgling, and severe diarrhoea that slows to a poorly formed, sometimes slimy stool in 4 to 5 days1517.

◦ These symptoms are likely due to an initial viral gastroenteritis, followed by prolonged allergic bowel inflammation and irritability with chronic sequelae1819.

• Other Reported Symptoms: Conjunctivitis, a variety of skin rashes, distal ischemic digit injuries, varied neurological symptoms, and symptoms of organ injury or failure1517.

Unusual Symptoms and Outcomes (challenging typical viral profiles)20...:

• Hypoxaemia poorly correlated to levels of dyspnoea2023.

• Sudden, rapidly progressive dyspnoea and SpO2 drop in an otherwise healthy patient, leading to poor outcomes2023.

• Slow chronic hypoxaemia with variable chronic lung damage from fibrosis over variable duration, often associated with a persistent, dry cough with or without wheezing2124.

• Mild SpO2 drop (not below 92%) that may require intermittent oxygen and usually resolves spontaneously in a few days to a week2124.

• Autopsy findings: Lungs are oedematous and heavy with microvascular clots; multiple organ involvement is usually due to hypoxic injury or DIC, or an immune/inflammatory response rather than direct viral infection2124.

• Chronic manifestations: COPD, Kawasaki-like illness in children, hypoxic injuries, thromboembolic injuries, and diabetes2225.

• Poor age and health status correlation: Fit, healthy young adults (25-year-olds) have succumbed suddenly, while high-risk elderly individuals (90-year-olds) recovered uneventfully2225.

• Patients with mild prolonged illness can present months later with chronic diseases like COPD and diabetes2225.

• Genetic predisposition/risk factors: Men are more at risk, with multiple intra-family fatalities (e.g., father/son deaths) related to increased infection risk and/or genetic predisposition. Varying mortality rates between countries and ethnicities have been observed2225.

• Children below 10 years old are least at risk2225.

Observations Regarding Treatment Protocols:

• The rapid response to medications used for Type 1 hypersensitivity reactions supports the existence of such a reaction in COVID-19 pathogenesis2627.

• Hydroxychloroquine initiated early can symptomatically help and suppress the hypersensitivity reaction around day 7, though it's less effective if started later428.

• Doxycycline used prophylactically in a high-risk group (160 teachers and police) showed fewer infections. Those who did get infected had mild transient symptoms, and their close contacts did not test positive or show symptoms, suggesting a suppressive effect on viral replication and transmission. However, three of these individuals still developed dyspnoea on day 7, which rapidly resolved with treatment2930.

• Montelukast: All 80 symptomatic patients who started montelukast in the first 7 days did not experience a reaction on day 7 or thereafter67.

• Promethazine effectively cleared chemical mediators, preventing lung damage and cytokine release, providing rapid relief from dyspnoea67.

• Prednisone, promethazine, and montelukast proved to be lifesaving, with no deaths or hospitalizations observed among over 200 patients treated67.

• The rapid and predictable outcomes achieved with these treatments, especially in severely ill patients, contrast with other medications like remdesivir, tocilizumab, or convalescent plasma, which have not shown such rapid responses and negated the need for oxygen and hospitalization in the author's observations2627.

• Monitoring for a hypersensitivity reaction and prompt treatment is believed to significantly decrease morbidity and mortality2627.

• Patients with mild to moderate initial illness are observed to develop tolerance with subsequent exposure2627.

• Asymptomatic individuals upon first exposure may become sensitized and be at risk of subsequent reactions2627.

These observations form the basis of the proposed two-aetiology model for COVID-19 and the corresponding treatment protocols1....

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Discuss Treatment Protocol.

The treatment protocol for COVID-19, as proposed by a KZN doctor based on over 200 symptomatic outpatient cases, is rooted in the understanding that COVID-19 illness has two overlapping etiologies: an initial respiratory viral infection and a later triggering of a Type 1 hypersensitivity reaction in sensitive individuals1.... This dual approach has led to "remarkable yet consistent and predictable results and recoveries," with no deaths or hospitalizations among the treated patients, even those with severe dyspnoea56. Notably, 12 severely dyspnoeic patients with SpO2 as low as 80% recovered to over 96% SpO2 within 24 to 36 hours of treatment, without the need for hospitalization or oxygen7.... All dyspnoeic patients achieved normal SpO2 within 3 days78.

The treatment strategy differs depending on the phase of the illness:

1. Viral Phase Protocol (Initial 7 days)

This phase is generally mild and self-limiting, with symptomatic treatment often being sufficient1112.

• Symptoms: Typically include sore throat, loss of smell and sweet/salty taste (bitter taste preserved), generalized body ache, fever with chills, dry persistent cough, a cold feeling between the shoulder blades, burning sensation in the chest, and tightness with scanty, clear sputum. Bacterial co-infection might present with a productive cough and purulent sputum, sinusitis, or earache1314.

• Drugs Used:

◦ Hydroxychloroquine: Has historical prophylactic use against viral infection and provides symptomatic benefit during the viral phase. If started early, it can also help suppress the hypersensitivity reaction that typically begins around day 73....

◦ Azithromycin: Recommended for bacterial bronchopneumonia complicating viral infections and bacterial upper respiratory tract infections (URTIs)1112.

◦ Doxycycline: Possesses a wide range of effects and, through its inhibitory effects on protein synthesis, may slow viral replication, potentially decreasing symptom severity and infectivity. It was used prophylactically in a large group of high-risk individuals, with observations suggesting a suppressive effect on viral replication and transmission11....

◦ Montelukast: Indicated for prophylaxis and treatment of atopic conditions, it has been used in this phase to prevent Type 1 reactions19....

• Protocol for Mild Symptoms: Hydroxychloroquine 200mg daily for 5 days, Montelukast 10mg daily for 1 month, and symptomatic treatment2024.

• Protocol for Moderate Symptoms: Hydroxychloroquine 200mg daily for 5 days, Azithromycin 500mg on day 1 then 250mg daily for 4 more days (or other appropriate antibiotic), Montelukast 10mg daily for 1 month, and symptomatic treatment2728.

• Patient Education: Patients are educated to recognize new symptoms from day 7 onwards, such as generalized body aches and pains, fatigue, dyspnoea, and decreasing SpO2, as these signal the start of the hypersensitivity reaction and require immediate reporting for treatment2728.

2. Hypersensitivity Phase Protocol (From Day 7 onwards)

This phase is triggered around the 7th day, probably by a viral protein fragment, leading to the release of chemical mediators and a variety of presentations and outcomes, including chronicity and complications if untreated2930.

• Symptoms: Can range from rapidly progressive dyspnoea with SpO2 dropping to the low 80s (with or without chest symptoms) to a slower, prolonged SpO2 decrease, persistent cough, and wheezing. Other reported symptoms during this period include rashes, neurological symptoms, and end-organ damage27....

• Drugs Used to Treat Type 1 Hypersensitivity Reactions:

◦ Prednisone: Indicated to suppress sudden onset severe allergic reactions and can be lifesaving when used from day 7 onwards. Its use in the first 7 days is generally detrimental and should be limited to life-threatening illnesses during that period22....

◦ Promethazine: The antihistamine of choice for Type 1 hypersensitivity reactions, it can rapidly and effectively suppress immediate manifestations and clear chemical mediators, providing rapid relief from dyspnoea and preventing lung damage and cytokine release19....

◦ Adrenaline (nebulized): Can be used immediately if severe dyspnoea or hypotension is suspected21....

◦ Montelukast: Continued use is recommended in this phase (10mg nocte for 1 month)2125.

◦ Aspirin: Used as prophylaxis2125.

◦ Naproxen: Used for fever, as it is considered to be from allergic inflammation rather than infection, with paracetamol alone noted as ineffective2125.

◦ Beclometasone (inhaled steroid): A topical steroid beneficial for patients with prolonged reactions and associated dry cough, potentially limiting lung fibrosis and progression to COPD20....

◦ Other less common drugs: Ipratropium bromide, sodium chromoglycate, and ketotifen may also provide benefit and possible prophylactic effects20....

• Protocol for Hypersensitivity Phase: Prednisone 50mg stat, then decreased by 5mg daily over the next 9 days (e.g., 50, 45, 40, 35mg in the morning). Lower doses tapered over a longer period may be needed for those with mild prolonged symptoms. Promethazine 25mg stat, then three times daily for 5 days. Adrenaline nebulization stat if severe dyspnoea or suspected hypotension. Aspirin prophylaxis daily for 1 month. Montelukast 10mg nightly for 1 month. Naproxen 250mg twice daily for fever. Beclometasone 200mcg inhaler twice daily for chronic dry cough21....

The rapid response to these medications used to treat Type 1 hypersensitivity reactions confirms its existence as a key element of COVID-19 pathogenesis3940. Monitoring for and promptly treating this hypersensitivity reaction is believed to significantly decrease morbidity and mortality3940. Identifying specific IgE levels might help identify individuals at risk of subsequent severe reactions and guide prophylactic and preventive treatment, potentially even negating the need for widespread vaccination21....

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Explain COVID's atypical symptom progression.

What triggers COVID's severe phase?

article briefedLIFELONG LEARNING

Virology

ABSTRACT

Elucidating the Pathogenesis and Rx of COVID Reveals a Missing Element

Currently there are few outpatient treatment recommendations, and there is a distinct lack of understanding of the disease progression. This is most likely due to the absence of sufficient outpatient examination, treatment and follow up because of isolation measures and current protocols. There is however a wealth of information around hospital presentations, investigations and pathological findings. Hospital treatment protocols are based on these findings, but have thus far not been universally consistent in efficacy and outcome. This has created controversy and confusion as to the pathogenesis and treatment of COVID.

Over the past five months, my staff and I have examined, treated and followed up on over 200 symptomatic COVID patients, some critically ill. In doing so, I used the information gathered to refine my understanding of the pathogenesis of COVID and thus adjust treatment protocols.

This has resulted in some remarkable yet consistent and predictable results and recoveries. In all, we have had no deaths, no hospitalisations and complete recoveries of all patients, even those with severe dyspnoea. Most confirmatory to my theory of the pathogenesis were the 12 most dyspnoeic patients with low

80% SpO2 that recovered to over 96% SpO2 within 24 to 36 hours of treatment, without the need for hospitalisation or oxygen. All dyspnoeic patients had normal SpO2 within 3 days of treatment.

The informat ion thus gathered can prevent most of the mortality and morbidity from COVID. The furthering of understanding of the pathogenesis of COVID can guide future research and intervention strategies to negate the effects of the pandemic.

Virus, detection and symptoms A RNA virus Airborne transmission. Common in stool samples? Waterborne transmission. The virus is highly contagious but infectivity and virulence are unknown due to a lack of understanding of the pathogenesis of COVID and testing limitations. The virus enters the cell through ACE 2 receptors. Like other common RNA viruses, it uses cell machinery to replicate and burst out copies, leaving behind dead cell debris and inflammation that could result in mild scarring. The average duration of symptoms is 3 to 6 days with the host being non-infective after day 7.

Laboratory detection Swabs vary greatly in their ability to isolate the virus due to technique used, training of screeners, the area swabbed etc. PCR tests are very specific but not very sensitive - about 65%, so about 35% false negatives - and so cannot be used for diagnosis or confirmation of diagnosis. It is only useful for screening purposes but not sensitive enough to guide detection and isolation/quarantine measures. Absolute numerical data is not a true reflection; ratios may yield a better insight Antibody testing may provide more reliable data.

Clinical presentation based on personal observations

• Infection of upper respiratory tract - sore throat, loss of smell, loss of sweet and salty taste, bitter preserved. Generalised body ache, fever with chills.

• Spreads lower - dry persistent cough, cold feeling between shoulder blades, burning sensation in chest, tightness with scanty, clear sputum.

• Bacterial co-infection - productive cough with purulent sputum, sinusitis with purulent mucus, earache etc. The above symptoms are progressive over the first 6 days of infection and may

This article is based on a KZN doctor’s experiences of treating COVID patients in an outpatient setting. His broad natural science background has afforded him a unique perspective of the pandemic, convincing him that something was missing. From the examination, treatment and follow up of over 200 symptomatic COVID patients, it is his opinion that COVID illness has two aetiologies, namely an initial respiratory viral infection with typical symptoms, progression and outcomes and a later triggering of a Type 1 hypersensitivity reaction in those that are sensitive. This article looks at the pathogenesis of COVID and his outpatient treatment protocols

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lead to a pneumonia with associated dyspnoea.

• A significant proportion of infected symptomatic individuals develop dyspnoea from day 7 onwards, irrespective of severity or duration of initial symptoms. Common associated symptoms are mild generalised body pain and fatigue to the point of having to sleep. This dyspnoea can be of sudden onset and rapidly progressive, leading to severe hypoxaemia and a SpO2 drop to below 85% in 2 days. It is more commonly insidious in onset and persistent for a variable duration, with SpO2 in the mid to low 90s, and may result in diffuse lung fibrosis the longer it persists. It is during this period that the rashes, neurologic symptoms and end organ damage are also reported.

• Gastrointestinal infection is common - usually preceded by a sore throat that spontaneously resolves in a day or two, heartburn, nausea, short severe intermittent abdominal cramps with tinkles and gurgling, severe diarrhoea that slows to a poorly formed, sometimes slimy stool in 4 to 5 days.

• O t h e r r e p o r t e d s y m p t o m s - conjunctivitis, a variety of skin rashes, distal ischemic digit injuries, varied neurologic symptoms, symptoms of organ injury or failure.

Case morphology Understanding the progression of this illness also requires an overview of the facts as they currently are occurring, compared to the facts as they are known to be.

Known facts Viruses are generally quite specific in the type of tissue they infect. Their infections are generally self-limiting, opportunistic and seldom cause death. Mortality is usually due to some other predisposition, either natural or chronic illness related.

Respiratory viruses cause symptoms ranging from none (most), to a mild sore throat which passes in a few days, or spreads lower, and can complicate with a bacterial infection ranging from mild bronchitis to pneumonia, with typical radiologic findings. These symptoms are

progressive and well understood, and these typical case presentations should be removed from analysis, to help concentrate on what is unknown.

Facts as they are occurring What remains are case histories that don’t fit the profile mentioned above, are atypical for a single virus, and don’t show typical disease progression and rates.

Unusual symptoms:

• Hypoxaemia poorly correlated to levels of dyspnoea. Sudden, rapidly progressive dyspnoea and SpO2 drop, in an otherwise healthy patient, resulting in poor outcomes.

• Slow chronic hypoxaemia with variable chronic lung damage from fibrosis over variable duration. Associated with a persistent, dry cough with or without wheezing.

• Mild SpO2 drop, not below 92% and may need intermittent oxygen. Usually resolves spontaneously in a few days to a week.

• A u t o p s y f i n d i n g s : L u n g s a r e o e d e m a t o u s a n d h e a v y w i t h microvascular clots. Multiple organ involvement usually due to hypoxic injury, DIC. Or, immune/inflammatory response rather than direct viral infection.

• Chronic mani festat ions : COPD, Kawasaki l ike i l lness in children, hypoxic injuries, thromboembolic injuries, diabetes.

Unusual outcomes: If we remove the usual risk-factor related outcomes that may complicate a typical viral infection, we are left with poor age and health status correlation. Fit, healthy 25 year olds have succumbed suddenly, and high risk 90 year olds got through uneventfully. Patients with mild prolonged illness can present back in a few months with chronic disease, commonly COPD, and diabetes. Men are more at risk with multiple intra-family fatalities related to increased risk of infection and or genetic predisposition. Many father/son deaths have occurred with the mother being spared, and vice versa, but less commonly. Varying

mortality rates between countries and ethnicities. Children below 10 years old are least at risk.

Pathogenesis from morphology It is clear from the case morphology that a viral infection alone cannot explain the diversity of symptoms, unusual presentations and unusual outcomes. Taking an overview using the wealth of information avai lable from the pathogenesis of a variety of conditions, may allow us to find the best fit for the unusual presentations and outcomes that are seen.

The only pathogenesis that fully explains these outcomes are Type 1 hypersensitivity reactions, the allergic reactions we have to external allergens, whether inhaled, ingested, or contacted. These reactions consist of an initial acute phase that lasts a few hours to a few days, and can be mild to fatal. They sometimes progress to a late phase reaction that lasts for a week or so, resulting in cell damage and other immune implications. Reactions to the same allergen vary in speed, severity, duration and symptoms, and if not treated, would have diverse outcomes, ranging from sudden anaphylactic type reactions leading to rapid deterioration and death, to moderate chronic allergic reactions resulting in scarring and collateral immune mediated injuries, to mild, transient, localised reactions.

In my op in ion , and f rom my examination, treatment and review of over 200 COVID patients, the initial Corona virus infection is like any other common respiratory virus infection, with a spread of statistics in similar ratios to previous epidemics, during the initial 7 days. On around the 7th day, a Type 1 hypersensitivity reaction is triggered in the lungs, probably due

to a recognisable viral protein fragment causing the release of chemical mediators, leading to the variety of presentations and outcomes that have been encountered, including chronicity and complications due to non-treatment. This reaction would not be directly related to age, comorbidities etc., but directly related to genetic predisposition and immune maturity, or lack thereof.

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I t m a y e x p l a i n t h e s u d d e n deterioration in lung oxygen exchange capacity and SpO2, in the asymptomatic and mild transient viral illness, at around the 7th day. The speed of deterioration varies greatly and can complicate an otherwise uneventful recovery of a high risk patient post day 7.

Those that have severe initial Type 1 reactions, presenting with sudden onset dyspnoea with steadily declining SpO2, can deteriorate rapidly and are at high risk of mortality. However, some with milder initial reactions that progress to late stage Type 1 hypersensitivity reactions present with persistent dry cough, symptoms of mild hypoxia or hypoxic injury etc, with mild but prolonged SpO2 drop. These will have varying degrees of lung damage over time.

Many of the reported chronic manifestations of COVID are explained by immune injury to the lungs (cytokine response) and col lateral immune or hypoxic injury to other organs or systems. The gastro intest ina l symptoms are likely due to an initial viral gastroenteritis, followed by a prolonged a l lerg ic bowel in f lammat ion and irritability, with chronic sequelae.

BCG vaccination and active PTB seem to modulate immunity and avert severe Type 1 reactions. Patients on immunomodulatory treatments are less likely to have a severe Type 1 reaction.

Children’s underdeveloped immunity is less likely to trigger a Type 1 reaction. Generally, younger patients will have no reactions due to it being their first exposure to the allergen. A reaction requires previous exposure. They will however, become sensitised, and subsequent exposure can provoke a more vigorous immune response. Those with mild to moderate initial reactions will become more tolerant to subsequent e x p o s u r e s . T h e y w i l l h o w e v e r , consequently become passive future transmitters of the virus.

Seeing that reports of reinfections are surfacing, a Type 1 reaction may provide an explanation for a prolonged second wave of infections with higher mortality in the younger population (sensitised individuals), and a shorter third wave with generally low mortality (tolerance) as per the Spanish Flu.

Treatment toolbox As I consider this disease to have two overlapping aetiologies, ie, viral and allergic, treatment would differ depending on the point at which it is initiated.

Outpatient drugs used so far H y d r o x y c h l o r o q u i n e h a s b e e n very controversial and has historic prophylactic use against viral infection, and has shown some prophylactic benefit in trials on healthcare workers. It has anti-inflammatory, antihistaminic, smooth muscle relaxant and antiarrhythmic properties. This could have symptomatic benefit during the viral phase of COVID illness. Its immunomodulatory effect would be of more benefit in the allergic reaction, but may be too slow in onset to be of benefit, if started well into the initial 7 days. The immunomodulatory effect of ivermectin may have a more rapid onset. • Azithromycin has shown benefits

in treating the usual and atypical bronchopneumonia complicating viral infections, and should be the antibiotic of choice in cases complicated by bacterial URTIs.

• Doxycycline has a wide range of effects, and through its inhibitory effects on protein synthesis, can potentially slow viral replication. This can potentially decrease symptom severity and infectivity of infected individuals.

• The viral phase of the il lness is generally mild and self-limiting and symptomatic treatment would be sufficient in most.

Drugs to treat Type 1 hypersensitivity reactions

• A d r e n a l i n e i s u s e d t o t r e a t hypovolemic shock. It can also be used to nebulise patients with rapidly progressive reactions and severe dyspnoea.

• Prednisone is indicated to suppress any sudden onset severe allergic reaction. Its use from day 7 onwards can be lifesaving. Use in the first 7 days can be detrimental and needs to be limited to life threatening illness in that period.

• Promethazine is the antihistamine of choice in Type 1 hypersensitivity

reactions. It can suppress all the immediate manifestations of Type 1 reactions rapidly and effectively. H2 antagonists may need to be added in those with gastrointestinal symptoms.

• Montelukast, a leukotriene receptor antagonist, blocks the effects of cysteinyl leukotrienes, a unique feature not achieved by corticosteroids. It has both bronchodilator and anti-inflammatory activity. It is indicated in the prophylaxis and treatment of atopic conditions, and has benefit in preventing Type 1 reactions.

• Beclometasone is an inhaled steroid that can suppress lung inflammation topically. It would be beneficial in patients with prolonged reactions with associated dry cough. It could also limit lung fibrosis and progression to COPD.

Other less common drugs that should have benefit are: ipratropium bromide / sodium chromoglycate/ ketotifen.

Protocol Viral phase Mild symptoms: Sore throat, loss of smell etc. • Hydroxychloroquine 200mg dly x 5

days • Montelukast 10mg dly x 1 month • Symptomatic treatment • Moderate symptoms: Present later into

illness so enquire about day of onset of symptoms - dry cough, mucopurulent bronchitis etc.

• Hydroxychloroquine 200mg dly x 5 days • Azithromycin 500mg on day 1, then

250mg dly for 4 more days, or other more appropriate antibiotic

• Montelukast 10mg dly x 1 month • Symptomatic treatment

Most patients recover quickly from mild symptoms. Those with moderate symptoms take a little longer.

All patients should be educated to be aware of new symptoms from day 7 onwards, even if completely well, and report immediately for treatment. These symptoms are usually: generalised body aches and pains, fatigue, dyspnoea and decreasing SpO2. These herald the start of the hypersensitivity reaction.

Elucidating the Pathogenesis and Rx of COVID Reveals a Missing Element

Hypersensitivity phase R a n g e o f p r e s e n t a t i o n : r a p i d l y progressive dyspnoea with SpO2 low 80% with or without chest symptoms to slow prolonged SpO2 decrease, prolonged cough, wheeze etc. • Prednisone 50mg stat and decrease

single dly morning dose by 5mg over next 9 days...50, 45, 40, 35mg mane... Those who present with mild prolonged symptoms may need lower doses tapered over a longer period.

• Promethazine 25mg stat then tds x 5 days.

• Adrenal ine nebs stat i f severe dyspnoea or if hypotension suspected

• Aspirin prophylaxis mane x 1 month. • Montelukast 10mg nocte x 1 month. • Naproxen 250mg bd for fever, as it is

from allergic inflammation, not infection. Paracetamol not effective alone.

• Beclate 200mcg inhaler bd for those with chronic dry cough (Topical steroid)

• Sodium Chromoglycate/ Ketotifen/ Ipratropium bromide inhaler may give better results and possible prophylactic benefit

Future infections Pat ients who do not deve lop a hypersensitivity reaction during the initial infection are either previously unexposed, or tolerant. Specific IgE screening would identify those at risk of subsequent reactions, and significantly elevated levels of IgE would identify those prone to severe reactions. Montelukast would prevent these reactions and should be used prophylactically in those with elevated IgE levels.

Observations The fo l low ing a re my persona l observations based on the examination of over 200 COVID patients, from presentation to full recovery, using the above treatment protocol. Many observations confirm the existence of a Type 1 hypersensitivity reaction.

Hydroxychloroquine and doxycycline Hydroxychloroquine initiated early helps symptomatically and can suppress the

hypersensitivity reaction on day 7. It is however less effective than other drugs in modulating immune hypersensitivity when started later on in the illness.

D o x y c y c l i n e h a s b e e n u s e d prophylactically in a large group (160) of high-risk individuals (teachers and police) over the past three months. Fewer individuals in the prophylaxis group have so far become infected, compared to their colleagues.

The four individuals that became infected had none to mild transient symptoms that resolved spontaneously during the viral phase. They were home isolated, with none of their close contacts testing positive or exhibiting symptoms over the duration of their illness. This may be indication of doxycycline’s suppressive effect on viral replication and consequently on viral transmission. However, three went on to develop dyspnoea on day 7 that resolved rapidly with treatment. Evaluation is ongoing.

All the other drugs used were dictated by bacterial infections and presenting symptoms, with their benefits reasonably obvious.

Patients presenting with dyspnoea or decreased SpO2 after day 7 were immediately started on treatment as outlined. All had improvement in symptoms and SpO2 within 24 hours. The most telling was a group of the 12 most hypoxic patients, who all presented after day 7, with SpO2 in the low 80%, all having severe dyspnoea etc. Every one of them had symptomatic relief within a few hours and returned to >96% SpO2 within 24 to 36 hours of starting treatment. This was achieved with outpatient treatment, on Room Air without the need for oxygen, and all 12 made full recoveries in a few days.

Montelukast, prednisone and promethazine All patients started on montelukast in the first 7 days had no reaction on day 7 or thereafter. (About 80 symptomatic patients)

Promethazine effectively cleared chemical mediators, thus preventing lung damage and the resultant cytokine release, giving rapid relief from dyspnoea.

Prednisone, promethaz ine and montelukast proved to be lifesaving, and after seeing over 200 COVID patients and

counting, we have not had a death, nor hospitalisation of a patient. All recovered completely within 14 days from onset.

No other medications in current use for the treatment of COVID 19 ie, remdesivir, tocilizumab, convalescent plasma etc, have shown such rapid response and predictable outcome in severely ill patients, negating the need for oxygen and hospitalisation.

Implications of observations The rapid response to the medications used to treat Type 1 hypersensitivity reactions confirms its existence. This could have some serious implications for the future management of the COVID pandemic.

Monitoring for a hypersensitivity reaction and prompt treatment would decrease morbidity and mortal i ty significantly. Those with mild to moderate initial illness will develop tolerance with subsequent exposure. However, those that were initially asymptomatic due to it being their first exposure, will become sensitised, and run the risk of subsequent reactions.

Identifying the specific IgE involved in this reaction and quantifying its levels would help identify those at risk. This would also help predict the severity of reaction to future exposure, and guide prophylactic and preventive treatment.

Vaccines against the virus would only benefit those that are hypersensitive, and blanket vaccinations would be unnecessary and unsafe in view of the rush to bring it to market without long term evaluation. Being able to identify hypersensitive individuals and provide appropriate information and treatment may negate the need for a vaccine altogether.

Conclusion With the high mortality and morbidity from COVID 19, it is my wish that the information presented above will help save lives and guide further research and management. The protocol and its deficiencies provide a valuable starting point for further evaluation of treatment interventions. I hope this brings some clarity during this difficult time.

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lead to a pneumonia with associated dyspnoea.

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Respiratory viruses cause symptoms ranging from none (most), to a mild sore throat which passes in a few days, or spreads lower, and can complicate with a bacterial infection ranging from mild bronchitis to pneumonia, with typical radiologic findings. These symptoms are

progressive and well understood, and these typical case presentations should be removed from analysis, to help concentrate on what is unknown.

Facts as they are occurring What remains are case histories that don’t fit the profile mentioned above, are atypical for a single virus, and don’t show typical disease progression and rates.

Unusual symptoms:

• Hypoxaemia poorly correlated to levels of dyspnoea. Sudden, rapidly progressive dyspnoea and SpO2 drop, in an otherwise healthy patient, resulting in poor outcomes.

• Slow chronic hypoxaemia with variable chronic lung damage from fibrosis over variable duration. Associated with a persistent, dry cough with or without wheezing.

• Mild SpO2 drop, not below 92% and may need intermittent oxygen. Usually resolves spontaneously in a few days to a week.

• A u t o p s y f i n d i n g s : L u n g s a r e o e d e m a t o u s a n d h e a v y w i t h microvascular clots. Multiple organ involvement usually due to hypoxic injury, DIC. Or, immune/inflammatory response rather than direct viral infection.

• Chronic mani festat ions : COPD, Kawasaki l ike i l lness in children, hypoxic injuries, thromboembolic injuries, diabetes.

Unusual outcomes: If we remove the usual risk-factor related outcomes that may complicate a typical viral infection, we are left with poor age and health status correlation. Fit, healthy 25 year olds have succumbed suddenly, and high risk 90 year olds got through uneventfully. Patients with mild prolonged illness can present back in a few months with chronic disease, commonly COPD, and diabetes. Men are more at risk with multiple intra-family fatalities related to increased risk of infection and or genetic predisposition. Many father/son deaths have occurred with the mother being spared, and vice versa, but less commonly. Varying

mortality rates between countries and ethnicities. Children below 10 years old are least at risk.

Pathogenesis from morphology It is clear from the case morphology that a viral infection alone cannot explain the diversity of symptoms, unusual presentations and unusual outcomes. Taking an overview using the wealth of information avai lable from the pathogenesis of a variety of conditions, may allow us to find the best fit for the unusual presentations and outcomes that are seen.

The only pathogenesis that fully explains these outcomes are Type 1 hypersensitivity reactions, the allergic reactions we have to external allergens, whether inhaled, ingested, or contacted. These reactions consist of an initial acute phase that lasts a few hours to a few days, and can be mild to fatal. They sometimes progress to a late phase reaction that lasts for a week or so, resulting in cell damage and other immune implications. Reactions to the same allergen vary in speed, severity, duration and symptoms, and if not treated, would have diverse outcomes, ranging from sudden anaphylactic type reactions leading to rapid deterioration and death, to moderate chronic allergic reactions resulting in scarring and collateral immune mediated injuries, to mild, transient, localised reactions.

In my op in ion , and f rom my examination, treatment and review of over 200 COVID patients, the initial Corona virus infection is like any other common respiratory virus infection, with a spread of statistics in similar ratios to previous epidemics, during the initial 7 days. On around the 7th day, a Type 1 hypersensitivity reaction is triggered in the lungs, probably due to a recognisable viral protein fragment causing the release of chemical mediators, leading to the variety of presentations and outcomes that have been encountered, including chronicity and complications due to non-treatment. This reaction would not be directly related to age, comorbidities etc., but directly related to genetic predisposition and immune maturity, or lack thereof.

LIFELONG LEARNING

Virology

I t m a y e x p l a i n t h e s u d d e n deterioration in lung oxygen exchange capacity and SpO2, in the asymptomatic and mild transient viral illness, at around the 7th day. The speed of deterioration varies greatly and can complicate an otherwise uneventful recovery of a high

risk patient post day 7.

Those that have severe initial Type 1 reactions, presenting with sudden onset dyspnoea with steadily declining SpO2, can deteriorate rapidly and are at high risk of mortality. However, some with milder initial reactions that progress to late stage Type 1 hypersensitivity reactions present with persistent dry cough, symptoms of mild hypoxia or hypoxic injury etc, with mild but prolonged SpO2 drop. These will have varying degrees of lung damage over time.

Many of the reported chronic manifestations of COVID are explained by immune injury to the lungs (cytokine response) and col lateral immune or hypoxic injury to other organs or systems. The gastro intest ina l symptoms are likely due to an initial viral gastroenteritis, followed by a prolonged a l lerg ic bowel in f lammat ion and irritability, with chronic sequelae.

BCG vaccination and active PTB seem to modulate immunity and avert severe Type 1 reactions. Patients on immunomodulatory treatments are less likely to have a severe Type 1 reaction.

Children's underdeveloped immunity is less likely to trigger a Type 1 reaction. Generally, younger patients will have no reactions due to it being their first exposure to the allergen. A reaction requires previous exposure. They will however, become sensitised, and subsequent exposure can provoke a more vigorous immune response. Those with mild to moderate initial reactions will become more tolerant to subsequent e x p o s u r e s . T h e y w i l l h o w e v e r , consequently become passive future transmitters of the virus.

Seeing that reports of reinfections are surfacing, a Type 1 reaction may provide an explanation for a prolonged second wave of infections with higher mortality in the younger population (sensitised individuals), and a shorter third wave with generally low mortality (tolerance) as per the Spanish Flu.

Treatment toolbox As I consider this disease to have two overlapping aetiologies, ie, viral and allergic, treatment would differ depending on the point at which it is initiated.

Outpatient drugs used so far H y d r o x y c h l o r o q u i n e h a s b e e n very controversial and has historic prophylactic use against viral infection, and has shown some prophylactic benefit in trials on healthcare workers. It has anti-inflammatory, antihistaminic, smooth muscle relaxant and antiarrhythmic properties. This could have symptomatic benefit during the viral phase of COVID illness. Its immunomodulatory effect would be of more benefit in the allergic reaction, but may be too slow in onset to be of benefit, if started well into the initial 7 days. The immunomodulatory effect of ivermectin may have a more rapid onset. • Azithromycin has shown benefits

in treating the usual and atypical bronchopneumonia complicating viral infections, and should be the antibiotic of choice in cases complicated by bacterial URTIs.

• Doxycycline has a wide range of effects, and through its inhibitory effects on protein synthesis, can potentially slow viral replication. This can potentially decrease symptom severity and infectivity of infected individuals.

• The viral phase of the il lness is generally mild and self-limiting and symptomatic treatment would be sufficient in most.

Drugs to treat Type 1 hypersensitivity reactions

• A d r e n a l i n e i s u s e d t o t r e a t hypovolemic shock. It can also be used to nebulise patients with rapidly progressive reactions and severe dyspnoea.

• Prednisone is indicated to suppress any sudden onset severe allergic reaction. Its use from day 7 onwards can be lifesaving. Use in the first 7 days can be detrimental and needs to be limited to life threatening illness in that period.

• Promethazine is the antihistamine of choice in Type 1 hypersensitivity

reactions. It can suppress all the immediate manifestations of Type 1 reactions rapidly and effectively. H2 antagonists may need to be added in those with gastrointestinal symptoms.

• Montelukast, a leukotriene receptor antagonist, blocks the effects of cysteinyl leukotrienes, a unique feature not achieved by corticosteroids. It has both bronchodilator and anti-inflammatory activity. It is indicated in the prophylaxis and treatment of atopic conditions, and has benefit in preventing Type 1 reactions.

• Beclometasone is an inhaled steroid that can suppress lung inflammation topically. It would be beneficial in patients with prolonged reactions with associated dry cough. It could also limit lung fibrosis and progression to COPD.

Other less common drugs that should have benefit are: ipratropium bromide / sodium chromoglycate/ ketotifen.

Protocol Viral phase Mild symptoms: Sore throat, loss of smell etc. • Hydroxychloroquine 200mg dly x 5

days • Montelukast 10mg dly x 1 month • Symptomatic treatment • Moderate symptoms: Present later into

illness so enquire about day of onset of symptoms - dry cough, mucopurulent bronchitis etc.

• Hydroxychloroquine 200mg dly x 5 days • Azithromycin 500mg on day 1, then

250mg dly for 4 more days, or other more appropriate antibiotic

• Montelukast 10mg dly x 1 month • Symptomatic treatment

Most patients recover quickly from mild symptoms. Those with moderate symptoms take a little longer.

All patients should be educated to be aware of new symptoms from day 7 onwards, even if completely well, and report immediately for treatment. These symptoms are usually: generalised body aches and pains, fatigue, dyspnoea and decreasing SpO2. These herald the start of the hypersensitivity reaction.

Elucidating the Pathogenesis and Rx of COVID Reveals a Missing Element

Hypersensitivity phase R a n g e o f p r e s e n t a t i o n : r a p i d l y progressive dyspnoea with SpO2 low 80% with or without chest symptoms to slow prolonged SpO2 decrease, prolonged cough, wheeze etc. • Prednisone 50mg stat and decrease

single dly morning dose by 5mg over next 9 days...50, 45, 40, 35mg mane... Those who present with mild prolonged symptoms may need lower doses tapered over a longer period.

• Promethazine 25mg stat then tds x 5 days.

• Adrenal ine nebs stat i f severe dyspnoea or if hypotension suspected

• Aspirin prophylaxis mane x 1 month. • Montelukast 10mg nocte x 1 month. • Naproxen 250mg bd for fever, as it is

from allergic inflammation, not infection. Paracetamol not effective alone.

• Beclate 200mcg inhaler bd for those with chronic dry cough (Topical steroid)

• Sodium Chromoglycate/ Ketotifen/ Ipratropium bromide inhaler may give better results and possible prophylactic benefit

Future infections Pat ients who do not deve lop a hypersensitivity reaction during the initial infection are either previously unexposed, or tolerant. Specific IgE screening would identify those at risk of subsequent reactions, and significantly elevated levels of IgE would identify those prone to severe reactions. Montelukast would prevent these reactions and should be used prophylactically in those with elevated IgE levels.

Observations The fo l low ing a re my persona l observations based on the examination of over 200 COVID patients, from presentation to full recovery, using the above treatment protocol. Many observations confirm the existence of a Type 1 hypersensitivity reaction.

Hydroxychloroquine and doxycycline Hydroxychloroquine initiated early helps symptomatically and can suppress the

hypersensitivity reaction on day 7. It is however less effective than other drugs in modulating immune hypersensitivity when started later on in the illness.

D o x y c y c l i n e h a s b e e n u s e d prophylactically in a large group (160) of high-risk individuals (teachers and police) over the past three months. Fewer individuals in the prophylaxis group have so far become infected, compared to their colleagues.

The four individuals that became infected had none to mild transient symptoms that resolved spontaneously during the viral phase. They were home isolated, with none of their close contacts testing positive or exhibiting symptoms over the duration of their illness. This may be indication of doxycycline's suppressive effect on viral replication and consequently on viral transmission. However, three went on to develop dyspnoea on day 7 that resolved rapidly with treatment. Evaluation is ongoing.

All the other drugs used were dictated by bacterial infections and presenting symptoms, with their benefits reasonably obvious.

Patients presenting with dyspnoea or decreased SpO2 after day 7 were immediately started on treatment as outlined. All had improvement in symptoms and SpO2 within 24 hours. The most telling was a group of the 12 most hypoxic patients, who all presented after day 7, with SpO2 in the low 80%, all having severe dyspnoea etc. Every one of them had symptomatic relief within a few hours and returned to >96% SpO2 within 24 to 36 hours of starting treatment. This was achieved with outpatient treatment, on Room Air without the need for oxygen, and all 12 made full recoveries in a few days.

Montelukast, prednisone and promethazine All patients started on montelukast in the first 7 days had no reaction on day 7 or thereafter. (About 80 symptomatic patients)

Promethazine effectively cleared chemical mediators, thus preventing lung damage and the resultant cytokine release, giving rapid relief from dyspnoea.

Prednisone, promethaz ine and montelukast proved to be lifesaving, and after seeing over 200 COVID patients and

counting, we have not had a death, nor hospitalisation of a patient. All recovered completely within 14 days from onset.

No other medications in current use for the treatment of COVID 19 ie, remdesivir, tocilizumab, convalescent plasma etc, have shown such rapid response and predictable outcome in severely ill patients, negating the need for oxygen and hospitalisation.

Implications of observations The rapid response to the medications used to treat Type 1 hypersensitivity reactions confirms its existence. This could have some serious implications for the future management of the COVID pandemic.

Monitoring for a hypersensitivity reaction and prompt treatment would decrease morbidity and mortal i ty significantly. Those with mild to moderate initial illness will develop tolerance with subsequent exposure. However, those that were initially asymptomatic due to it being

their first exposure, will become sensitised, and run the risk of subsequent reactions.

Identifying the specific IgE involved in this reaction and quantifying its levels would help identify those at risk. This would also help predict the severity of reaction to future exposure, and guide prophylactic and preventive treatment.

Vaccines against the virus would only benefit those that are hypersensitive, and blanket vaccinations would be unnecessary and unsafe in view of the rush to bring it to market without long term evaluation. Being able to identify hypersensitive individuals and provide appropriate information and treatment may negate the need for a vaccine altogether.

Conclusion With the high mortality and morbidity from COVID 19, it is my wish that the information presented above will help save lives and guide further research and management. The protocol and its deficiencies provide a valuable starting point for further evaluation of treatment interventions. I hope this brings some clarity during this difficult time.

text of lm podcast

Welcome, curious minds, to another fascinating journey into the depths of understanding.

Great to be here.

Today, we're embarking on a truly unique deep dive. And right up front, welcome to the Lenny and Maria Sanchez deep dive podcast show.

Yeah, this one's quite something.

We're diving into an intriguing exploration. It's a doctor's firstirhand experience treating CO 19 patients, and they believe they've uncovered a crucial missing element in understanding the disease.

Our mission today really is to give you a shortcut to understanding this well groundbreaking perspective on co 19's pathogenesis and treatment straight from the source material

right based on direct clinical observation.

So let's start by highlighting a critical gap the source identifies. This really shaped the doctor's unique perspective didn't it? A distinct lack of understanding and recommendations for outpatient COVID treatment.

Exactly. It seems like a lot of the focus understandably perhaps was on hospitalized patients but that meant outpatient care especially with isol measures was well less understood.

Patients weren't always examined closely or followed up on outside the hospital.

That's the point made in the source. While there was loads of data from hospitals, pathology reports, the protocols weren't always consistent in their results. It led to um quite a bit of confusion.

Yeah.

So, this source drawing on a doctor in KZN's experience with I think over 200 symptomatic COVID patients treated outside the hospital.

Yeah.

It offers a really different angle trying to fill that gap by watching closely and tweaking treatments.

And this next observation, it really challenges the conventional narrative, doesn't it?

It certainly does.

This doctor makes an extraordinary claim based on their refined understanding and these adjusted protocols. No deaths, no hospitalizations, and complete recoveries of all patients. That includes people who came in with severe breathing difficulties.

Yeah, that's a powerful statement. Really flies in the face of a lot of early experiences. Suggests a fundamentally different approach was working for them

and they offer some pretty compelling evidence. Right.

They do. The most striking example, the one they felt confirmed their theory involved 12 severely dysoic patients. Dystoic meaning, you know, struggling significantly to breathe.

Right?

These patients had oxygen saturation levels. It's B2. How much oxygen's in the blood? Down around 80%. Which is quite low.

Definitely concerning.

But they recovered. Got back over 96% P2 within, get this, 24 to 36 hours of treatment. without hospitalization,

without hospitalization, without needing extra oxygen. All dispoic patients they report hit normal SPO2 levels within 3 days. That specific clinical result was key to their whole hypothesis.

Wow. Okay. So, let's back up a bit. What did the source say about the virus itself, its basic characteristics?

Well, the basics are there. It's an RNA virus, mainly airborne transmission. Okay.

Though, interestingly, the source notes it was often found in stool samples. So, they floated the idea of possible waterborne transmission, too. Though, uh how infeious. It was that way. It wasn't really clear back then. Limitations in testing and understanding the full picture, you know,

right? Early days.

And on a cellular level, it gets in using those AC2 receptors. Standard stuff for some viruses.

It hijacks the cell's machinery

pretty much. Replicates itself, bursts out, leaves behind dead cell debris, causes inflammation. The source mentions this could lead to mild scarring if it's widespread.

And how long do the viral symptoms typically last? According to this source,

usually about 3 to six days for the main viral symptoms. Yeah.

And the person was generally considered non-infective after day seven. That helps define that initial phase, the purely viral part.

Now, diagnostics, the source highlighted some real challenges there, didn't it? Especially with swabs.

Oh, absolutely. Huge variability in how well swabs actually isolated the virus. It wasn't just about the virus, but things like the technique, how well the person doing the swab was trained, even where they swabbed, made accurate early detection tricky.

So, inconsistent results,

very And then there's the critique of PCR tests. The source notes, they're specific. If it finds the virus, it's there, no doubt. But the sensitivity only about 65%. Which means roughly 35% false negatives.

35%. That's quite high.

It is. Think about it.

Yeah.

Great for confirming a positive, but if you get a negative, there's a significant chance it's wrong. It could miss a lot of infections.

So relying on PCR alone for diagnosis or deciding who needs to isolate, problematic.

That's the argument in the source. It makes PCR useful for screening large groups maybe, but not reliable enough on its own for individual diagnosis or guiding quarantine. The absolute numbers from PCR tests might not have reflected the true scale. Antibbody testing, they suggest, might offer a clearer picture of past infection rates.

Makes sense. Okay, let's take symptom progression. The doctor observed a pattern, right?

Yes, a fairly clear one based on their clinical observations. It starts typically in the upper respiratory tract,

like a sore throat.

Sore throat. Yeah. And that distinctive loss of smell and loss of sweet and salty tastes. But interestingly, bitter taste often remained. Plus, general body aches, fever, chills. Pretty standard start for many viral things.

But then it moved.

Then it often spread lower down into the respiratory tract leading to a dry, persistent cough. Sometimes a weird cold feeling between the shoulder blades,

a burning sensation in the chest, tightness,

sometimes a little bit of clear sputum, but not much.

And bacterial co- infections. Were those distinct? Yes, they presented differently. Yeah, more like a productive cough, thicker appear in sputum, sinusitis symptoms, ear ache sometimes.

The source emphasizes this progression usually happens over the first six days. That's the initial viral phase playing out.

Okay. Day six. Then comes day seven. The source highlights this as a critical turning point, especially regarding breathing difficulties, the dispoa.

Exactly. A large proportion of symptomatic patients, regardless of how bad their initial symptoms were, started developing breathing problems from 7 onwards.

Regardless of initial severity, that's interesting.

It is. It suggests something changes around that time. Almost like a switch flips in how the body is responding.

And this despo It wasn't always the same.

No. The source describes two main forms they saw clinically. One was sudden onset got worse very quickly. SPO2 could plummet below 85% in just a couple of days. That's severe hypoxmia.

Scary.

Definitely. The other form was more common apparently. More insidious, slower onset, persistent breathing. difficulty, but the SPO2 might hover in the mid to low 90s.

Still not great, but not that sudden drop,

right? But the worry with this slower kind, if it lasted a while, was the potential for diffuse lung fibrosis, scarring,

and other symptoms appear around this time, too, after day seven.

Yeah, that's when other systemic things often showed up. Crashes, neurological issues, signs of endorgan damage. It wasn't just about the lungs anymore.

You mentioned GI issues earlier as well.

Yes, gastrointestinal infection was reported as common. Often it started after a sore throat. It had already come and gone.

Strange sequence

a bit. Yeah. Symptoms like heartburn, nausea, really intense but short abdominal cramps described with tingles and gurgling and then severe diarrhea which would eventually slow down over four or five days

and other things.

All sorts reported conjunctivitis, various skin rashes, those weird distal eskeemic digit injuries, COVID toes people talked about and other neurological or organ specific injury symptoms. It really paints a picture of disease that could manifest in so many different ways, way beyond a typical cold or flu virus.

So, the source then explicitly contrasts this with typical viruses.

It does. It lays out the known facts. Viruses usually stick to specific tissues. They're self-limiting, rarely fatal, unless you have underlying conditions. Respiratory viruses cause familiar patterns, maybe leading to bacterial bronchitis or pneumonia sometime.

Understood progressions,

right? The source suggests that if you mentally remove those typical viral presentations from the equation, what you're left with is the truly unusual stuff about CO

and that leftover picture, it didn't look like a single virus acting alone

exactly. The remaining case histories, the unusual outcomes, they just didn't fit the profile. Atypical for a single virus, as the source puts it, didn't follow expected patterns or rates. This divergence, this mismatch is what drove the doctor's search for another explanation.

The inconsistencies were a clue.

Precisely.

And this is where for me it gets really interesting. The unusual symptoms and outcomes that just didn't line up with conventional views.

Yeah. Like the hypoxmia, low blood oxygen that didn't always match how breathless the patient felt or seemed.

Happy hypoxia, some called it

kind of. And those sudden rapid drops in SPO2 and otherwise healthy people leading to bad outcomes unexpectedly. Plus the chronicity issue long-term problems like COPD developing later, Kawasaki like illness in kids, new onset diabetes,

and the outcomes defying risk factors.

That's the really baffling part. noted in the source fit 25-year-olds dying suddenly while some high-risisk 90-year-olds sailed through it. People with mild illness developing chronic conditions months later

and the family clusters.

Yeah. Multiple deaths within families like father and son hinting at maybe a genetic risk, some predisposition, plus differing mortality rates across countries, ethnicities, and always kids under 10 being least at risk.

It all points away from just a simple virus host interaction, doesn't it?

It raises serious questions about individual susceptibility bi ological differences, things beyond just age and co-orbidities.

Okay, so let's unpack the core theory, the missing element. What is it?

The source is pretty clear. A viral infection alone can't explain all this diversity, these unusual patterns and outcomes. The proposed explanation, type one hypersensitivity reactions,

basically allergic reactions

essentially. Yes, common allergic reactions. That's identified as the key to understanding the discrepancies. A real potential gamecher in perspective. explain that type one reaction a bit more.

Okay, so type one reactions have an initial phase. Can be hours to days, mild to life-threatening. Sometimes they progress to a late phase lasting maybe a week causing cell damage.

Right?

The sourc's opinion based on their clinical work is that the initial COVID infection acts like a normal respiratory virus for those first 6 days or so.

But then

but then around day seven, something triggers a type one hypersensitivity reaction in the lungs. Likely a viral protein fragment acts as the allergen.

An allergen produced by the virus nurse itself.

Effectively, this triggers a rapid release of chemical mediators, histamine, lucotrines, the stuff your body releases in an allergic reaction causes inflammation symptoms.

And this explains the variability.

That's the theory. This reaction is linked more to your genetic predisposition, your immune system's maturity or lack thereof, rather than just age or health status. That could explain the huge range presentations, the weird outcomes, the chronicity, the complications. It's not just the virus, it's the allergic response to the virus in susceptible people.

How does the immune system fit into prevention or reinfection under this model? The source mentioned BCG and TB.

Yeah, it suggests things like BCG vaccination or active TB seem to modulate the immune system in a way that might actually avert these severe type 1 reactions. A protective effect perhaps.

Interesting. And what about kids versus adults or reinfection?

So, the idea is children, their immune systems aren't fully developed. They're less likely to mount this big type one reaction on their first exposure to the allergen, the viral fragment,

but they get sensitized.

They get sensitized. Exactly. So, future exposures could be different.

Conversely, people who have only a mild reaction initially might develop tolerance, making later exposures less severe.

So, this could explain epidemic waves.

Potentially, this type one reaction model could explain, say, a second wave hitting younger, now sensitized people harder, maybe with higher mortality, then perhaps a third wave being shorter, less deadly as population tolerance builds. The source draws a parallel to patterns seen in the Spanish flu. It offers a different mechanism for understanding those waves,

right? A different lens. Okay. Treatment. Based on this dual idea virus, then hypersensitivity, the source proposed a two-pronged approach for outpatients. What about the viral phase first?

For the initial viral phase, the strategy involved drugs that might inhibit the virus, reduce symptoms, or maybe have anti-inflammatory effects.

Hydroxychloroquin was mentioned, noted for historical use against viruses. and its known anti-inflammatory anti-histamatic muscle relaxing properties. The idea was it could provide symptomatic relief during that viral phase. Athramycin, an antibiotic was found useful for bacterial co- infections which can complicate viral illnesses. Standard practice really

and doxycycline

doxycycline another antibiotic was considered because it might potentially slow viral replication by inhibiting protein synthesis. This could maybe lessen symptoms and infectivity.

It was reportedly used prophylactically in some high-risisk groups with anecdotal observations of maybe lower infection rates among them.

Okay, so that's addressing the initial viral part. Now the really crucial bit, the drugs targeting the proposed type 1 hypersensitivity reaction. This seems key to those claimed results.

Absolutely. This is where the protocol gets very specific, targeting that allergic pipe response from day seven onwards.

What drugs were used?

Adrenaline often used for shock, but here used via nebulizer for patients crashing quickly with severe dysmoa. Radnosone, a steroid, very important, indicated to suppress those sudden, severe allergic reactions from day seven onwards. The source stresses using it before day seven could be detrimental unless someone was critically ill. Timing is everything,

right? Treat the right phase.

Exactly. Then promethazine, a potent antihistamine. This was used to clear out those chemical mediators, histamine, etc. Giving rapid relief from the breathing difficulty.

And Montaluc.

Montaluc blocks lucatrines, another set of chemical mediators that steroids don't hit as well. It was used to prevent the type one reaction from really taking off

prophylactically almost

or early in the reaction. And finally, beclaone, an inhaled steroid used directly in the lungs to suppress inflammation, help with persistent coughs, and potentially limit that fibrosis or progression to COPD.

It's a very targeted cocktail for that specific reaction phase.

Highly targeted, based entirely on the hypersensitivity theory.

And the source reports observations that seem to confirm this. worked.

Yes. Strong confirmations from their perspective. Patients started on Montlucas within the first seven days reportedly just didn't have the reaction on day seven or later. This was seen in about 80 patients.

Wow.

Promethazine gave rapid relief, suggesting it was clearing those mediators effectively. And the combination predisones Montaluc was described flat out as life-saving

leading to the no deaths, no hospitalizations claim among their 200 plus patients.

That's the report. All recovered completely, typically within 14 days of symptoms starting using this protocol targeting the presumed type 1 reaction.

So the rapid response to these allergy focused meds is presented as proof the reaction exists.

That's the interpretation in the source. Yes, it confirms its existence and the implications if this holds true are huge for future pandemics.

How so?

Well, monitoring patients specifically for signs of this hypersensitivity reaction around day seven and treating it promptly with these kinds of drugs could dramatically cut down illness severity and deaths. and screening.

They even suggest identifying people prone to this reaction using specific allergy tests that could allow for prophylactic treatment to prevent the severe phase. And the source goes so far as to suggest this approach might even negate the need for a vaccine altogether for some by managing the allergic component.

That's a very provocative statement

extremely. It really challenges the mainstream approach.

Okay, so let's try and summarize this deep dive. We've explored a doctor's quite unique perspective. on CO 19 proposing this dual pathogenesis initial virus then a critical type 1 hypersensitivity reaction kicking in around day seven.

Right. A theory born from outpatient observation.

And this theory led to a specific outpatient treatment protocol focusing heavily on managing that allergic type reaction with uh truly remarkable results claimed for their patient cohort. No deaths, no hospitalizations.

Yeah. Complete recoveries reported for over 200 patients. It's a compelling if perhaps specific data set.

So a final thought for you the listener

maybe consider how challenging established medical thinking even based on observations from smaller specific groups like this can be really valuable. It can spark critical rethinking about how diseases work and how we might treat them differently. It underscores the importance of really looking at patients and adapting, doesn't it?

Continuous learning and observation in action. Definitely food for thought. Thank you for listening to another session of the Lenny and Maria Sanchez deep dive podcast show produced and archived at the website Daily info.

Summary

This source introduces a groundbreaking theory regarding COVID-19, suggesting that beyond the initial viral infection, a Type 1 hypersensitivity reaction (an allergic response) is the "missing element" responsible for severe illness and complications starting around day seven. Based on firsthand outpatient treatment of over 200 symptomatic patients, a doctor developed a two-pronged treatment protocol; one for the initial viral phase and another, critically, for the allergic phase. The source claims this approach yielded no deaths, no hospitalizations, and complete recoveries, even for patients with severe breathing difficulties, highlighting the rapid reversal of symptoms with allergy-focused medications as compelling evidence for this allergic component. This perspective challenges conventional

understanding by suggesting that the body's overreaction, rather than just the virus itself, drives the disease's varied and severe manifestations, potentially offering a new paradigm for treatment and future pandemic preparedness.

The provided sources describe a unique approach to COVID-19 treatment based on a doctor's personal observations and experience with over 200 symptomatic COVID patients in an outpatient setting in KZN1.... This approach is built upon a theory that the disease has a "missing element" in its pathogenesis, which, when understood and targeted, leads to highly effective outcomes4....

Understanding COVID-19 Pathogenesis: The Dual Aetiology Theory The central premise guiding this treatment approach is that COVID-19 illness has two overlapping aetiologies:

• Initial Viral Infection: This phase is similar to other common respiratory viral infections, typically lasting the first 6-7 days with characteristic symptoms and outcomes1.... The virus, an RNA virus, primarily spreads through airborne transmission and enters cells via ACE2 receptors, replicating and causing cell damage and inflammation9.... Symptoms during this phase include sore throat, loss of smell and taste (sweet and salty), generalized body ache, fever with chills, and a dry persistent cough that may spread lower into the respiratory tract10.... Bacterial co-infections, leading to productive cough and purulent sputum, can also occur in this phase10....

• Triggering of a Type 1 Hypersensitivity Reaction: Around day 7 onwards, in sensitive individuals, a Type 1 hypersensitivity (allergic) reaction is triggered in the lungs1.... This reaction is believed to be caused by a recognizable viral protein fragment acting as an allergen, leading to the release of chemical mediators and a diverse range of presentations and outcomes7.... This allergic response is suggested to be related to genetic predisposition and immune maturity, rather than age or comorbidities, explaining unusual symptoms and outcomes that a viral infection alone cannot7.... This phase is associated with new symptoms like generalized body aches, fatigue, and dyspnoea (breathing difficulty) with decreasing SpO220....

COVID-19 Treatment Protocol Given this dual aetiology, the treatment protocol differs depending on the stage of the illness2728.

1. Viral Phase (First 6 Days) The viral phase is generally mild and self-limiting, with symptomatic treatment often being sufficient2930.

• Hydroxychloroquine: Recommended at 200mg daily for 5 days. It has historic prophylactic use against viral infection, and possesses anti-inflammatory, antihistaminic, smooth muscle relaxant, and antiarrhythmic properties, which can provide symptomatic benefit. When started early, it can also help suppress the hypersensitivity reaction on day 7, though it's less effective for immune hypersensitivity if initiated later in the illness24....

• Azithromycin: Recommended at 500mg on day 1, then 250mg daily for 4 more days, or another appropriate antibiotic. It is beneficial for treating typical and atypical bronchopneumonia that complicates viral infections, and is the antibiotic of choice for bacterial upper respiratory tract infections (URTIs)24....

• Doxycycline: Can potentially slow viral replication by inhibiting protein synthesis, which may decrease symptom severity and infectivity. It was used prophylactically in a group of 160 high-risk individuals (teachers and police), with observations suggesting fewer infections and milder, transient symptoms in those who did get infected, along with reduced viral transmission29....

• Montelukast: Recommended at 10mg daily for 1 month24....

Patients are educated to be aware of new symptoms from day 7 onwards, even if they feel well, as these herald the start of the hypersensitivity reaction and require immediate treatment2426.

2. Hypersensitivity Phase (From Day 7 Onwards) This phase targets the Type 1 hypersensitivity reaction, which can range from rapidly progressive dyspnoea with low SpO2 (e.g., low 80%) to slow, prolonged SpO2 decrease and chronic cough3940.

• Prednisone: A corticosteroid, indicated to suppress sudden onset severe allergic reactions. Its use from day 7 onwards is considered life-saving. However, using it in the first 7 days can be detrimental and should be limited to life-threatening illness during that period. The protocol suggests 50mg stat, then decreasing by 5mg daily over the next 9 days39....

• Promethazine: An antihistamine, is the antihistamine of choice for Type 1 hypersensitivity reactions. It can rapidly and effectively suppress all immediate manifestations of these reactions, clear chemical mediators, prevent lung damage, and provide rapid relief from dyspnoea. Recommended at 25mg stat, then three times daily for 5 days39....

• Adrenaline (Epinephrine): Used via nebulizer immediately ("stat") if there is severe dyspnoea or suspected hypotension, similar to its use for hypovolemic shock41....

• Montelukast: A leukotriene receptor antagonist, blocks cysteinyl leukotrienes (a unique feature not achieved by corticosteroids). It has bronchodilator and anti-inflammatory activity, preventing Type 1 reactions. Recommended at 10mg nightly for 1 month44.... Notably, patients started on montelukast in the first 7 days reportedly experienced no reaction on day 7 or thereafter47....

• Beclometasone: An inhaled steroid that topically suppresses lung inflammation. It is beneficial for patients with prolonged reactions and associated dry cough, and could limit lung fibrosis and progression to COPD. Recommended at 200mcg inhaler twice daily31....

• Other Medications:

◦ Aspirin: Prophylaxis, once daily for 1 month4950.

◦ Naproxen: 250mg twice daily for fever, as the fever is attributed to allergic inflammation rather than infection, and paracetamol alone is not effective4950.

◦ H2 antagonists: May be added for those with gastrointestinal symptoms4546.

◦ Ipratropium bromide, Sodium Chromoglycate, Ketotifen: Other less common drugs that may offer benefit and possible prophylactic effects31....

Observed Outcomes and Implications The doctor's approach, based on treating COVID-19 as an initial viral infection followed by a Type 1 hypersensitivity reaction, has reportedly yielded "remarkable yet consistent and predictable results and recoveries"5253.

• Zero Mortality and Hospitalizations: Among over 200 symptomatic COVID patients treated, there were no deaths and no hospitalizations, with complete recoveries for all patients, including those with severe dyspnoea47....

• Rapid Recovery from Hypoxia: Twelve severely dyspnoeic patients with low SpO2 (around 80%) recovered to over 96% SpO2 within 24 to 36 hours of outpatient treatment, without needing hospitalization or oxygen12.... All dyspnoeic patients achieved normal SpO2 levels within 3 days1213.

• Confirmation of Hypersensitivity: The rapid and effective response to medications typically used to treat Type 1 hypersensitivity reactions (like prednisone, promethazine, and montelukast) is presented as confirmation of the existence of this allergic component in COVID-19 pathogenesis47.... These medications were described as "lifesaving" and showed a "rapid response and predictable outcome in severely ill patients," surpassing other medications in current use for COVID-19 (e.g., remdesivir, tocilizumab, convalescent plasma) in negating the need for oxygen and hospitalization47....

These observations have significant implications, suggesting that monitoring for and promptly treating a hypersensitivity reaction could significantly decrease COVID-19 morbidity and mortality55.... Identifying individuals at risk through specific IgE screening could guide prophylactic and preventive treatment, potentially even negating the need for a vaccine altogether for some by effectively managing the allergic component62....

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Discuss Allergic Reaction Theory.

The Allergic Reaction Theory, as presented in the sources, proposes a dual pathogenesis for COVID-19, suggesting that the illness is not solely a viral infection but also involves a Type 1 hypersensitivity reaction1.... This theory was developed by a KZN doctor based on observations from examining, treating, and following up on over 200 symptomatic COVID patients in an outpatient setting1....

Here's a breakdown of the theory:

Rationale for the Theory (The "Missing Element"): The doctor's perspective arose from a perceived lack of understanding of COVID-19 disease progression and few outpatient treatment recommendations, primarily due to isolation measures and current protocols limiting outpatient examination and follow-up13.... While there was extensive hospital data, treatment protocols based on these findings were not consistently effective, leading to controversy and confusion regarding COVID-19 pathogenesis and treatment12....

The theory aims to explain unusual symptoms and outcomes that do not fit the profile of a typical viral infection16...:

• Hypoxemia (low blood oxygen) poorly correlated with levels of dyspnoea16....

• Sudden, rapidly progressive dyspnoea and SpO2 (oxygen saturation) drops in otherwise healthy patients, leading to poor outcomes16....

• Slow, chronic hypoxemia with variable chronic lung damage from fibrosis2021.

• Chronic manifestations such as COPD, Kawasaki-like illness in children, hypoxic injuries, thromboembolic injuries, and diabetes19....

• Poor correlation with age and health status, where fit, healthy young individuals might succumb suddenly, while high-risk elderly patients recover uneventfully19....

• Family clusters of fatalities (e.g., father/son deaths), suggesting genetic predisposition22....

• Varying mortality rates between countries and ethnicities, and children under 10 being least at risk5....

Mechanism of the Type 1 Hypersensitivity Reaction: The theory posits that the initial Corona virus infection behaves like any other common respiratory virus infection during the first 6-7 days4.... However, around the 7th day, a Type 1 hypersensitivity reaction is triggered in the lungs4....

• This reaction is likely caused by a recognizable viral protein fragment acting as an allergen, leading to the release of chemical mediators4....

• Unlike the viral infection, this allergic reaction is not directly related to age or comorbidities but is instead linked to genetic predisposition and immune maturity4....

• This mechanism can explain the sudden deterioration in lung oxygen exchange capacity and SpO2 drop that occurs around day 7, even in patients who had initially asymptomatic or mild viral illness3132. The speed of this deterioration can vary greatly3132.

• It also accounts for the various presentations and outcomes, including chronicity and complications due to non-treatment4....

• Reported chronic manifestations of COVID-19 are explained by immune injury to the lungs (cytokine response) and collateral immune or hypoxic injury to other organs3334.

• Gastrointestinal symptoms are attributed to an initial viral gastroenteritis, followed by prolonged allergic bowel inflammation and irritability, potentially leading to chronic sequelae33....

Influence on Disease Progression:

• A significant proportion of infected symptomatic individuals develop dyspnoea from day 7 onwards, regardless of the initial symptoms' severity27....

• This dyspnoea can be sudden and rapidly progressive, leading to severe hypoxemia and a SpO2 drop below 85% within two days27....

• More commonly, it is insidious in onset and persistent, with SpO2 in the mid to low 90s, potentially resulting in diffuse lung fibrosis if it persists longer27....

• Rashes, neurological symptoms, and end-organ damage are also commonly reported during this hypersensitivity phase27....

Immunity and Future Reactions:

• BCG vaccination and active tuberculosis appear to modulate immunity and may avert severe Type 1 reactions33....

• Children's underdeveloped immunity makes them less likely to trigger a severe Type 1 reaction on their first exposure to the allergen38.... However, they may become sensitized, meaning subsequent exposures could provoke a more vigorous immune response38....

• Individuals with mild to moderate initial reactions may develop tolerance to subsequent exposures39....

• This model can potentially explain epidemic waves, such as a prolonged second wave with higher mortality in a younger, now sensitized population, followed by a shorter third wave with lower mortality as tolerance builds, drawing a parallel to the Spanish Flu7....

• Patients who do not develop a hypersensitivity reaction are either previously unexposed or tolerant43....

Treatment Implications based on the Theory: Given the two overlapping etiologies (viral and allergic), treatment protocols differ based on the phase of the illness742. The doctor developed specific outpatient treatment protocols, particularly for the hypersensitivity phase1....

• For the hypersensitivity phase (from day 7 onwards), drugs targeting Type 1 hypersensitivity reactions are crucial:

◦ Adrenaline: Used via nebulizer for rapidly progressive reactions and severe dyspnoea44....

◦ Prednisone: A steroid indicated to suppress sudden, severe allergic reactions. Its use from day 7 onwards can be lifesaving, but its use in the first 7 days is generally considered detrimental unless the illness is life-threatening46....

◦ Promethazine: An antihistamine used to rapidly and effectively suppress immediate manifestations of Type 1 reactions by clearing chemical mediators, providing quick relief from dyspnoea46....

◦ Montelukast: A leukotriene receptor antagonist that blocks effects not achieved by corticosteroids. It has bronchodilator and anti-inflammatory activity and is beneficial in preventing Type 1 reactions. The source reports that all 80 symptomatic patients started on Montelukast in the first 7 days had no reaction on day 7 or thereafter28....

◦ Beclometasone: An inhaled steroid that topically suppresses lung inflammation, useful for prolonged reactions and chronic dry cough, and can limit lung fibrosis44....

Reported Outcomes and Confirmation: The doctor's clinical experience with over 200 symptomatic COVID patients using this protocol yielded remarkable, consistent, and predictable results: no deaths, no hospitalizations, and complete recoveries of all patients, even those with severe dyspnoea10....

• Notably, 12 severely dyspnoeic patients with SpO2 levels in the low 80s recovered to over 96% SpO2 within 24 to 36 hours of treatment without the need for hospitalization or oxygen63.... All dyspnoeic patients achieved normal SpO2 within 3 days6364.

• The rapid response to medications used to treat Type 1 hypersensitivity reactions is presented as confirmation of its existence45....

• The source suggests that this protocol showed more rapid response and predictable outcomes in severely ill patients compared to other current COVID-19 medications like remdesivir, tocilizumab, or convalescent plasma, negating the need for oxygen and

hospitalization4568.

Implications for Future Management: If this theory holds true, monitoring patients for hypersensitivity reactions and prompt treatment could significantly decrease morbidity and mortality45....

• Identifying individuals at risk through specific IgE screening could help predict the severity of future reactions and guide prophylactic treatment, such as using Montelukast9....

• The source controversially suggests that vaccines might only benefit hypersensitive individuals, and blanket vaccinations could be unnecessary and potentially unsafe given the rushed development without long-term evaluation6970.

• Furthermore, the ability to identify hypersensitive individuals and provide appropriate treatment might negate the need for a vaccine altogether9....

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Discuss Outpatient Care.

Outpatient care for COVID-19 is a key focus of the provided sources, which highlight a significant gap in understanding and recommendations for this setting1....

Here's a breakdown of the information regarding outpatient care:

1. The Initial Gap in Outpatient Understanding:

• There was a distinct lack of understanding of disease progression and few outpatient treatment recommendations for COVID-191....

• This was largely attributed to the absence of sufficient outpatient examination, treatment, and follow-up, primarily due to isolation measures and existing protocols1....

• While a wealth of information existed from hospital presentations and findings, hospital treatment protocols were not universally consistent in efficacy or outcome, leading to confusion1....

2. A Doctor's Outpatient-Centric Approach:

• A doctor in KZN, drawing on his broad natural science background, sought to fill this gap4....

• Over five months, he and his staff examined, treated, and followed up on over 200 symptomatic COVID patients in an outpatient setting, including some critically ill individuals4....

• This direct clinical observation allowed him to refine his understanding of COVID-19 pathogenesis and adjust treatment protocols4....

3. Remarkable Outcomes of the Outpatient Protocol:

• The refined outpatient treatment protocols led to remarkable, consistent, and predictable results and recoveries78.

• The doctor reported no deaths, no hospitalizations, and complete recoveries of all patients, even those with severe dyspnoea7....

• A particularly compelling example involved 12 severely dyspnoeic patients with SpO2 levels as low as 80%, who recovered to over 96% SpO2 within 24 to 36 hours of outpatient treatment. Crucially, this was achieved without the need for hospitalization or oxygen13.... All dyspnoeic patients reportedly achieved normal SpO2 within 3 days13....

• Overall, all patients treated with this protocol recovered completely within 14 days from the onset of symptoms910.

4. The Outpatient Treatment Protocol: The protocol is based on the theory that COVID-19 has two overlapping etiologies: an initial viral infection and a later Type 1 hypersensitivity (allergic) reaction1718. Treatment differs depending on the phase:

• Viral Phase (Initial 3 to 6 days, generally mild and self-limiting)13...:

◦ Hydroxychloroquine (200mg daily x 5 days) for symptomatic benefit, anti-inflammatory, and antihistaminic properties; it can also suppress the hypersensitivity reaction if started early17....

◦ Montelukast (10mg daily x 1 month) for prophylaxis and prevention of Type 1 reactions22....

◦ Azithromycin (500mg on day 1, then 250mg for 4 more days) or another appropriate antibiotic for bacterial co-infections17....

◦ Doxycycline was considered for its potential to slow viral replication and reduce symptom severity and infectivity. It was used prophylactically in high-risk groups, with anecdotal observations of lower infection rates and milder symptoms in those who did get infected19....

◦ Patients are educated to be aware of new symptoms (generalized body aches, fatigue, dyspnoea, decreasing SpO2) from day 7 onwards, as these herald the start of the hypersensitivity reaction3031.

• Hypersensitivity Phase (From day 7 onwards, for dyspnoea and SpO2 drop)35...:

◦ Prednisone (50mg stat, then tapered daily over 9 days) is crucial for suppressing sudden, severe allergic reactions. Its use from day 7 onwards can be lifesaving, but it should be limited in the first 7 days to life-threatening illness36....

◦ Promethazine (25mg stat, then three times daily for 5 days) is the antihistamine of choice, effectively and rapidly suppressing immediate manifestations of Type 1 reactions and clearing chemical mediators, providing rapid relief from dyspnoea9....

◦ Adrenaline nebulizers (stat) are used for severe dyspnoea or suspected hypotension40....

◦ Montelukast (10mg nightly x 1 month) blocks leukotrienes, helping to prevent Type 1 reactions9.... Patients started on montelukast in the first 7 days reportedly did not develop the hypersensitivity reaction (about 80 patients)9....

◦ Aspirin prophylaxis (once daily for 1 month)4344.

◦ Naproxen (250mg twice daily) for fever, as it's attributed to allergic inflammation rather than infection4344.

◦ Beclometasone (200mcg inhaler twice daily) is an inhaled steroid to topically suppress lung inflammation, beneficial for prolonged reactions with dry cough, potentially limiting lung fibrosis and progression to COPD22....

◦ Other less common drugs mentioned for benefit include ipratropium bromide, sodium chromoglycate, and ketotifen22....

5. Implications for Future Outpatient Management:

• The rapid response to medications typically used for Type 1 hypersensitivity reactions is presented as confirmation of this reaction's existence in COVID-1946....

• Monitoring for a hypersensitivity reaction and prompt outpatient treatment could significantly decrease morbidity and mortality46....

• Identifying individuals at risk through specific IgE screening could guide prophylactic and preventive treatment. The source even suggests that this approach might negate the need for a vaccine altogether for some by effectively managing the allergic component of the disease49....

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Discuss Symptom Progression.

Based on the provided sources, the symptom progression of COVID-19, as observed by the KZN doctor treating over 200 symptomatic patients, is understood to have two distinct overlapping etiologies: an initial viral infection followed by a Type 1 hypersensitivity reaction1....

Here is a detailed breakdown of the symptom progression:

• Initial Viral Phase (First 6 Days):

◦ The illness typically begins with symptoms affecting the upper respiratory tract5....

◦ Common initial symptoms include a sore throat, loss of smell, and loss of sweet and salty taste, though bitter taste often remains preserved5....

◦ Patients may also experience generalised body aches, fever with chills5....

◦ According to the source, the average duration of these main viral symptoms is typically 3 to 6 days, and the host is generally considered non-infective after day 78....

◦ The virus, an RNA virus, is primarily transmitted airborne and enters cells via ACE2 receptors, replicating and causing cell debris and inflammation8....

• Spread and Bacterial Co-infections:

◦ The infection can then spread lower into the respiratory tract, leading to a dry, persistent cough, a cold feeling between the shoulder blades, and a burning sensation in the chest with scanty, clear sputum5....

◦ Bacterial co-infections are also observed, presenting differently with a productive cough producing purulent sputum, sinusitis with purulent mucus, or earache5.... These symptoms are generally progressive over the first six days of infection56.

• Critical Turning Point: Hypersensitivity Phase (From Day 7 Onwards):

◦ A significant proportion of infected symptomatic individuals develop dyspnoea (breathing difficulties) from day 7 onwards, irrespective of the severity or duration of their initial symptoms13.... This suggests a shift in the body's response around this time15.

◦ This dyspnoea can manifest in two main ways:

▪ Sudden onset and rapidly progressive: Leading to severe hypoxaemia and a SpO2 (oxygen saturation) drop to below 85% in 2 days13.... This is described as very concerning16.

▪ More commonly insidious in onset and persistent: With SpO2 in the mid to low 90s, which may result in diffuse lung fibrosis the longer it persists13....

◦ During this period (from day 7 onwards), other systemic symptoms are also reported, including rashes, neurologic symptoms, and end-organ damage13....

◦ The doctor's opinion is that around the 7th day, a Type 1 hypersensitivity reaction is triggered in the lungs, likely due to a viral protein fragment acting as an allergen, leading to the diverse presentations and outcomes, including chronicity17.... This allergic reaction, rather than the viral infection alone, is proposed to explain the sudden deterioration in lung oxygen exchange capacity and SpO22021.

• Gastrointestinal and Other Symptoms:

◦ Gastrointestinal infection is common, often preceded by a sore throat that resolves spontaneously in a day or two22....

◦ GI symptoms include heartburn, nausea, short severe intermittent abdominal cramps with tinkles and gurgling, and severe diarrhoea that eventually slows to a poorly formed, sometimes slimy stool in 4 to 5 days22.... These are likely due to an initial viral gastroenteritis followed by prolonged allergic bowel inflammation2526.

◦ Other reported symptoms include conjunctivitis, a variety of skin rashes, distal ischemic digit injuries (like "COVID toes"), and varied neurologic symptoms, or symptoms of organ injury or failure22....

• Atypical Presentation and Outcomes (Contrasting with Known Viral Behavior):

◦ The observed progression in COVID-19 includes unusual symptoms and outcomes that do not fit the profile of a typical single viral infection27....

◦ These include hypoxaemia poorly correlated to levels of dyspnoea ("happy hypoxia"), sudden and rapidly progressive dyspnoea and SpO2 drop in otherwise healthy patients, and slow chronic hypoxaemia potentially leading to lung fibrosis27....

◦ Autopsy findings often reveal oedematous and heavy lungs with microvascular clots, and multiple organ involvement, often due to hypoxic injury or an immune/inflammatory response rather than direct viral infection3031.

◦ Chronic manifestations like COPD, Kawasaki-like illness in children, hypoxic injuries, thromboembolic injuries, and diabetes are also reported32....

◦ Unusual outcomes include poor age and health status correlation (e.g., healthy young adults succumbing suddenly while high-risk elderly recover uneventfully), and patients with mild prolonged illness developing chronic conditions months later32.... Familial fatalities (e.g., father/son deaths) hint at genetic predisposition33....

This multi-phase progression, particularly the distinct turning point around day 7 and the atypical symptoms/outcomes, led the doctor to propose the Type 1 hypersensitivity reaction as the "missing element" in understanding COVID-19 pathogenesis1....

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Discuss Diagnostic Challenges.

The sources highlight several diagnostic challenges related to COVID-19, particularly concerning early detection and the reliability of testing methods1.... These challenges significantly impacted the understanding of disease progression and the ability to guide isolation and treatment measures effectively4....

Key diagnostic challenges include:

• Variability in Swab Effectiveness: The ability of swabs to isolate the virus varied greatly. This was influenced by factors such as the technique used for swabbing, the training of the screeners, and even the specific area swabbed1.... This inconsistency made accurate early detection difficult3.

• Limitations of PCR Tests:

◦ Specificity vs. Sensitivity: While PCR tests are highly specific (meaning if the virus is found, it's definitely there), their sensitivity was only about 65%1....

◦ High False Negative Rate: This low sensitivity translates to approximately 35% false negatives1.... A significant chance of a negative result being incorrect meant that many infections could be missed8.

◦ Inadequacy for Diagnosis/Quarantine: Due to this high false-negative rate, PCR tests could not be reliably used for definitive diagnosis or confirmation of diagnosis1.... They were considered useful mainly for screening purposes, but not sensitive enough to guide individual

detection, isolation, or quarantine measures effectively1....

◦ Misleading Numerical Data: The sources suggest that absolute numerical data from PCR tests might not have been a true reflection of the situation, and ratios might offer better insight1....

• Potential for Undiagnosed Cases: The limitations of PCR testing meant that the true scale of infection might have been underestimated due to missed cases8.

• Role of Antibody Testing: The sources suggest that antibody testing might provide more reliable data regarding past infection rates, offering a clearer picture than PCR alone1....

The difficulty in accurate and consistent diagnosis contributed to a lack of understanding of COVID-19 pathogenesis and disease progression, especially in outpatient settings, which also led to controversy and confusion regarding treatment approaches4....

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